BUREAU OF HYGIENE AND TROPICAL DISEASES

BULLETIN OF HYGIENE

Volume 35, No. 6 June, 1960

Public Health

The order in this section is:—**General; Vital Statistics; Epidemiology; Maternal and Child Health; Health of Students, Nurses and Hospital Staffs; Health of Old Persons and the Chronically Ill; Chronic Cardio-Respiratory Diseases; Chronic Rheumatism; Cancer; Miscellaneous Diseases; Dental Health; Mental Health.**

GENERAL

WORLD HEALTH ORGANIZATION. PUB. HEALTH PAPERS No. 3. **Health Services in the USSR. Report prepared by the Participants in a Study Tour.** 58 pp., 5 diagrams. 1960. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [3s. 6d.; $0.60; Sw.fr. 2.–.]

This report was compiled individually and collectively by the 23 members of a group who, at the invitation of the World Health Organization, visited the U.S.S.R. in October 1958 to study its health services. The countries and territories represented by the study group were 21 in number and are listed in an appendix. An extensive itinerary was arranged by the Government of the U.S.S.R. to visit institutions in Moscow, Leningrad, Kiev, Tbilisi, Sukhumi and Tashkent during the stay of a little over 5 weeks.

The report which is short but clearly written deals under separate headings with the general organization and salient features of the health services; medical care; maternal and child health; communicable diseases; non-communicable and chronic diseases; occupational health; environmental sanitation; sanatoria, rest homes and health resorts; medical education and paramedical training; research and laboratories; health education; mental health; and vital and health statistics. There are several appendices which present some diagrams of the structure of some of the health services.

These health services designed to secure integration of curative and preventive aspects have been developed during the past 40 years and have as their basic principle "highly centralized planning and supervision, coupled with almost complete executive and operational decentralization" and "are available to the whole population free of charge, regardless of social and economic status". These services are given a general description. It is of interest to note that all heads of departments and divisions are medical graduates. The posts of sanitary engineer, sanitary inspector, social worker and social anthropologist are unknown in the U.S.S.R. Administration in relation to public health and hospitals is performed by doctors. The total number of doctors in the U.S.S.R. has increased from 23,000 in 1913 to 360,000 in 1957, of whom about half are women.

There are some points of special interest in the section on maternal and child health. The maternal death rate in 1957 was only 5 per 10,000 births. Antenatal and post-partum maternity leaves, each of 56 days, are legally provided for. Psycho-prophylaxis in regard to painless childbirth has been extended and was used in 60% of urban and 40% of rural confinements in 1957. Abortion for social, economic or health reasons has again been legalized at a fixed fee of 50 roubles but it is not generally encouraged. It is stressed that no stigma is attached to unmarried mothers. The practice of swaddling of infants is still widely employed. Not less than 91% of all infants are breast-fed and breast-milk banks are maintained. Vaccination against smallpox and with BCG is compulsory. Immunization against diphtheria and pertussis is a routine measure.

In the sections on diseases it is stated that for many years no cases of plague, cholera, smallpox, relapsing fever, typhus or dracunculosis have occurred. The incidence of malaria has been greatly reduced from 9·5 million cases in 1934 to only 5,000 in 1957. The "morbidity rate of tuberculosis has been reduced by 41% since 1950, and is at present 300 per 100,000". Helminthiasis is still an important problem. Cardiovascular disease is the most important cause of death and there is an increase in hypertensive disease and myocardial infarction. Rheumatic fever is a most important disease and in 1957 its morbidity rate in children was 3·4%.

The cancer problem is being tackled in several ways. "Prophylactic oncological screening of the whole population has become a routine" and from 1945–57 the cancer morbidity rate in more than 100 million persons was found to be between 110 and 170 per 100,000. The registration of every cancer case is compulsory. Cancer of the stomach is the most common form (33%) of the disease. Under the heading of nutritional disorders it is stated that the problem of these does not exist in the U.S.S.R.

There is a good account of medical training which is now 6 years in length and of the instruction of paramedical staff which includes nurses, midwives and of "feldschers". These feldschers have "played an important part in the health services of Russia even since the middle of the nineteenth century" and at one time undertook virtually the whole care of the rural population.

In a short but interesting section on mental health it is stated that the "mental health problem in the U.S.S.R. does not appear to be of sufficient magnitude to warrant any widespread measures". Neuroses and psychoneuroses are said to be rare. No mental health or child guidance clinics exist. The study group, who did not visit any psychiatric institutes or hospitals, state in their report that "The low morbidity rate of psychoneuroses is officially attributed to the 'sheltered' life of the population and the complete absence of unemployment in the country".

The statistical section gives the following: the birth rate in 1957 was 25·3, the death rate 7·8 as compared with 18·3 in 1940 and the infant mortality per 1,000 live births was 45 as compared with 184 in 1940.

M. E. Delafield

LI, Teh-Chuan. **Ten Years of Public Health Work in New China.** *Chinese Med. J.* Peking. 1959, Dec., v. 79, No. 6, 483–8.

The author sums up the advances made during the period since the Chinese Communist Party came into power. The general line was to go all out, to aim high and to get greater, quicker, better and more economical results to build socialism. Prevention of disease was a primary task, and there was close cooperation between medical personnel trained in western schools and the practitioners of traditional medicine. The key tasks were to eliminate mosquitoes, flies, rats and grain-eating sparrows, to promote social and personal hygiene and to aim at "health improvement and socialist construction".

Extensive claims are made. Schistosomiasis has now been practically eradicated from 65% of the once-affected areas; malaria from 39% and kala azar from 90%. "Apart from the national minority areas, the whole country is now freed from the menace of such venereal diseases as symptomatic syphilis and acute gonorrhoea." This theme is elaborated and supported by figures and information illustrating the growth of medical education and of the provision for the sick. On the information presented the change in this short period seems to have been prodigious; the credit is given to the general acceptance of socialist ideas, and to the party wh introduced them. *Charles Wilcock*

HSÜ, Yun-Pei. **Cooperation between Traditio Chinese and Western Medicine to prom People's Health.** *Chinese Med. J.* Peking. 19 Dec., v. 79, No. 6, 489–92.

Modern China recognizes the fact that a traditio system of medicine has existed for thousands of ye and that it has its virtues—so much so that full-ti classes in traditional medicine for western-style doct have recently been increased from 6 to 30. Many m western-style doctors study the system in their sp time, and the traditionalists are busily training appr tices (52,000 in 1958). 305 hospitals with over 7, beds, and about 950 clinics of traditional medicine h been established, and departments of traditional m cine have been established in all big hospitals. T traditionalists have their own theories of physiol and treatment, and these are the subjects of resea [It is not, apparently, simply a matter of gradu inducing the traditionalists to accept western ideas.] *Charles Wilcock*

HOU, Tsung-Ch'ang, CHUNG, Huei-Lan, HO, Lien-Yi WENG, Hsin-Chih. **Achievements in the Fi against Parasitic Diseases in New China.** *Chi Med. J.* Peking. 1959, Dec., v. 79, No. 6, 493–5 [252 refs.]

This paper deals with epidemiological studies, clin and therapeutic studies, and studies on preventive curative measures. In the first section there is a s statement of the great amount of survey work w has been done, and emphasis is placed upon the provement in the condition of the mass of the pe which has been brought about by the socialist appro to health problems.

In the second part an account is given of the deve ment of clinical work in recent years, in diagnosis treatment. Much of this is on conventional lines, the authors make a feature of several traditi remedies, including areca nut. The section on pre tion is largely conventional. There seems to be doubt that the attack on schistosomiasis is energ and determined. "Such achievements in such a s period of time would be utterly impossible under capitalist system. Eradication of the five para diseases in China is no longer in question." T include malaria, filariasis, kala azar and hookw infections. [This paper, like the 2 which precede i written in excellent English.] *Charles Wilcoc*

HEALTH OF STUDENTS, NURSES AND HOSPITAL STAFFS

CARPENTER, R. G. **Statistical Analysis of Suicide and other Mortality Rates of Students.** *Brit. J. Preventive & Social Med.* 1959, Oct., v. 13, No. 4, 163–74, 1 fig. [18 refs.]

The suicide rate among male Cambridge and Oxford undergraduates during the post-war period has been about 3 times that of the combined rate for 7 o British Universities or the general male populatio comparable age. There is no evidence that the sui rate for Cambridge undergraduates has undergone change during the past 35 years. At Cambridge 1 the 23 suicides during 1923–48 occurred in term-

and during 1948–58 all the 13 suicides occurred in term-time. Of the 30 suicides in term-time 11 occurred in the 1st, 15 in the 2nd and 3 in the 3rd and 1 in the 4th years of residence. Although there is a suggestion that suicide may be associated with examinations in the 2nd year there is nothing to suggest an association with the final examinations. The suicide rate for women students is insignificantly larger than the rate for women aged 20–24. The calculation of the general death rate presents difficulties but it appears that the undergraduate population has a lower death rate from diseases than the general population of the same ages. The author discusses the possible defects in his data. *W. J. Martin*

HEALTH OF OLD PERSONS AND THE CHRONICALLY ILL

RICHARDSON, I. M., BRODIE, A. S. & WILSON, Sarah. **Social and Medical Needs of Old People in Orkney. Report of a Sample Survey.** *Health Bull.* (Issued by the Chief M.O., Dept. of Health, Scotland.) 1959, Oct., v. 17, No. 4, 75–9.

A sample survey of elderly people living in the City of Aberdeen and within 15 to 20 miles outside it is now under way. It is a medical and sociological study intended to cover "all aspects of older people's lives". The present paper describes a similar study conducted in Orkney which it was thought might be useful.

The sample of "old people" defined as those who gave their age as over 65 was obtained by selecting every tenth such person in the files of each general practitioner in the Orkney group of islands. The total of persons ultimately available for study was 233 of whom 91 were male and 142 female. Almost all these were interviewed in their own homes wherever possible, and all by the same health visitor who had been appointed for this field work which was often arduous when the outer islands had to be visited. At the interview which usually lasted nearly an hour information was obtained on (1) health, (2) family, (3) occupation, (4) leisure, (5) accommodation, (6) use of services and (7) unmet needs and recommendations. The information obtained which has not yet been fully analysed is described in this preliminary report. Tables set out the findings in respect of: capacity for movement (classified as unlimited, limited outside the house, housebound and bedfast) by age and sex; medical attendance and mobility; and loneliness by sex, by mobility and by living arrangements.

"The overall pattern that emerges from this limited survey is much as might have been expected. On the whole medical and social services are working well and there were almost no signs of the dire poverty, neglected disabilities, and social breakdowns so common a few decades ago." Nevertheless much could be done to improve the lot of some of the old people and recommendations are made about home helps, expansion of voluntary services and special housing.

M. E. Delafield

WARREN, M. D. **The Hospital Resettlement Clinic and the Community Care of Handicapped People.** *Med. Officer.* 1960, Feb. 5, v. 103, No. 6, 69–74. [23 refs.]

This paper is an account of a hospital resettlement clinic established at the Royal Free Hospital, London in early 1959: it developed from one started in 1948.

The earlier part of the article sets out in detail the objectives of such a clinic and gives references to the somewhat meagre information available as to the size of the problem. It has been estimated that "between 10 and 20 per cent. of all patients discharged from general hospitals will have to accept some fundamental change in their way of life at work and/or at home". The objectives are summarized as (1) to enable the patient to cope with the routine activities of daily life such as eating, urination, defaecation, washing, dressing and locomotion; (2) to provide recreational and social activities and contacts, and (3) to provide employment by training for paid work or for routine housework.

In theory there are excellent services for handicapped people but they are uneven in their distribution and the main deficiencies are "Failure to develop adequate services *in the country as a whole* and failure of communication", *i.e.* between the various services, statutory or voluntary, engaged in different parts of what is the same field.

It should be the duty of the doctor in charge of the patient to initiate resettlement and to mobilize the after-care services. The need for a clinic arises from the variety of people whose help is required.

The clinic is held once a week. The patients are referred to it by the hospital consultants. The key person is the chairman who must be medical and may be a consultant in physical medicine or in orthopaedics, the local MOH or a doctor from the department of social medicine. All new patients are seen by the chairman who, after consulting his colleagues, decides who should be invited to a case conference. The chairman and the hospital almoner attend every conference: others who may be called upon to attend include the clinical consultant concerned or his registrar, the general practitioner, the ward sister, the industrial medical officer of the patient's firm, the physiotherapist, the occupational therapist, representatives, sometimes at both field and administrative levels, of the relevant departments of the local authority, the disablement resettlement officer of the Ministry of Labour, someone from the National Assistance Board and from any voluntary organizations concerned. It is a formidable list but they are never all needed for the same conference. The case conference agrees on who would be most acceptable and useful as the home visitor. Follow-up, to ensure that effective action is taken, is essential.

Details of two interesting and difficult cases are given. *Allen Daley*

CHRONIC CARDIO-RESPIRATORY DISEASES

FAIRBAIRN, A. S., WOOD, C. H. & FLETCHER, C. M. **Variability in Answers to a Questionnaire on Respiratory Symptoms.** *Brit. J. Preventive & Social Med.* 1959, Oct., v. 13, No. 4, 175–93, 2 figs.

In recent years estimates of the prevalence of respiratory symptoms have been made in several population groups by means of interviews between research workers and all (or random samples of all) members of such groups. Questionnaires have been developed for this purpose and usually these are completed by one observer at one interview with each subject. Epidemiological studies often demand comparisons between population groups and, because such comparisons will include interviews made by more than one observer, the authors designed the present experiment in order to compare several observers in their use of a detailed standardized questionnaire.

Each of 288 post office workers was interviewed twice at an interval of 6 weeks. At each interview the same questionnaire was used by one of 6 observers (3 doctors and 3 health visitors). The design of the experiment allowed for a larger number of subjects, in case any originally chosen would not co-operate or were not available for both interviews; in fact less than 5% replacement was required. The 288 subjects comprised 8 samples of 36 post office workers drawn from 8 strata of the total population of 1,070 postmen and women sorters aged 40–59 years who were based on a London, E.C. District Office. The strata were determined by dividing the population into 4 groups by age (40–49 and 50–59) and sex, drawing a random sample from each group and dividing each sample into 2 equal parts according to the extent of the recorded sickness absence from respiratory disease of the subjects in the sample.

The questionnaires and written briefing instructions are given in appendices to the paper and a table shows the allocation of subjects to observers. In effect 48 subjects (6 from each stratum) were questioned by the same observer at each interview while 240 were questioned by different observers at each interview; every combination and sequence of pairs of observers was equally represented in each stratum and all allocations of subjects to observers were otherwise made at random. The main results of the analysis of the completed questionnaires are given in a table and corresponding diagram. The proportion of positive replies received to each of 24 questions by each observer is shown. The design of the experiment made it possible to adjust these proportions to eliminate differences between observers attributable to the fact that they were interviewing different subjects.

As a result of 4 questions, 4 significant ($P < 0{\cdot}05$) differences in the prevalence of symptoms were found between the reports of the doctors and the health visitors when these were considered as 2 homogeneous groups. The differences ranged from 5 to 10% of subjects interviewed. As a result of 3 questions, 4 significant differences were found between individual doctors in the prevalence rates derived from their reports; these differences ranged from 15 to 19%. As a result of 7 questions, 9 significant differences we found between individual health visitors in the p valence rates obtained from their reports; these diff ences ranged from 8 to 19% of subjects interview The table shows a number of other differences whi are large though not significant by the authors' chos criterion of $P < 0{\cdot}05$. [It would have been help to the reader if the error variances on which t significance tests were based had been included so t this table could have been given the detailed conside tion which it deserves.]

Tape recordings were made of the interviews order to find out the reasons for disagreement betwe the 2 answers obtained from the same subject to same question. 160 such disagreements were chos at random from the answers to 12 questions wh had yielded significantly different prevalence ra between observers. Examples are quoted from th to illustrate failures on the part of the interview to keep to the rules of briefing. 149 other disagr ments drawn at random were similarly examin 62% of these were considered to be due to the obser in that at one of the interviews the question was incorrectly or the answer misunderstood; 21% appea to be due to the subject giving quite different answ to the same question when it was put correctly a the remaining 16% were considered to be due to question yielding borderline answers which could be clarified within the permitted briefing rules. general, failure by observers to obey the rules to overstatement of the number of positive answers

The authors conclude with a discussion of t results and make suggestions for decreasing obser variability in future surveys. [In view of the size the observer variation revealed by this experiment, report requires careful consideration by all resea workers who contemplate prevalence surveys us interview techniques. Much more research of kind is required to achieve the uniformity necess before prevalence rates obtained by different in viewers in the field can be compared with confiden The authors have, with others, prepared the gro for further research by agreeing upon a questionn and instructions for its use which appear to them be the best in the light of present knowledge". questionnaire will shortly be published.

E. A. Cheesema

KIDD, C. W. & PARK, A. T. **Bronchitis in the Insu Population of Northern Ireland.** *Brit. J. Pre tive & Social Med.* 1959, Oct., v. 13, No. 4, 211

This study was based on a 20% sample of the from National Insurance sources for the 3 y 1955–7. The incidence of bronchitis was about times higher for married women than for males for other women the rate was about 80% of the r rate. The inception rate among males stea increased with age and the rate at 60–64 during

3 years was 2–3½ times larger than at ages 15–19. The trend of the female rate with age was rather erratic but tended to increase slightly with age. Married women had longer spells of sickness from bronchitis than the other 2 groups, males and other women. Spells of bronchitis lasting longer than one year, per 1,000 exposed to risk, were 1·3 for other women, 2·5 for males and 4·8 for married women. *W. J. Martin*

CANCER

HOWE, G. M. **The Geographical Distribution of Disease with special reference to Cancer of the Lung and Stomach in Wales.** *Brit. J. Preventive & Social Med.* 1959, Oct., v. 13, No. 4, 204–10, 7 figs. [24 refs.]

The observed deaths in 1947–53 in each administrative area of Wales are compared with those expected at the age-specific death rates of England and Wales for cancer of the lung and bronchus in men and cancer of the stomach in women. The resulting standardized mortality ratios are shown in maps. Cancer of the lung is higher in the more densely populated areas though in almost all it is less than the expected figure for England and Wales. Even these areas appear to be remarkedly free from air pollution. A map of bright sunshine does not suggest an inverse relationship with cancer of the lung.

Cancer of the stomach shows a rural distribution and might conceivably be related to the water supply with its acidity and organic matter from peat soils and other undesirable constituents. The paper is not, however, intended to contribute to knowledge of cancer causation but to make a plea for this geographical approach with maps depicting the distribution of different variables. *A. Bradford Hill*

OLSEN, H. C. & GILSON, J. C. **Respiratory Symptoms, Bronchitis, and Ventilatory Capacity in Men. An Anglo-Danish Comparison, with special reference to Differences in Smoking Habits.** *Brit. Med. J.* 1960, Feb. 13, 450–56, 1 diagram. [28 refs.]

The respiratory symptoms, past medical history and smoking habits were recorded for 183 men (91% of a random sample of 200) aged 55–64 and living in the small town of Rønne in the island of Bornholm. Various physical and physiological measurements were also made. The results can be compared with those previously reached by HIGGINS and COCHRAN using identical methods in rural areas of South Wales and Scotland [this *Bulletin*, 1958, v. 33, 238; 1959, v. 34, 238]. In the Rønne group there was a strikingly lower frequency of such symptoms as cough, sputum, cough and sputum, or wheeze. There was also a lower incidence of asthma, chronic bronchitis and chest illness with cough and sputum in previous years, but not of pneumonia or pleurisy. Breathlessness as clinically graded was about half as frequent in Rønne. The physiological measurements showed a significantly higher average ventilatory capacity in the Danish group. The cause of these differences is unlikely to lie in air pollution which is absent from all the areas, and the climatic differences are not large.

There is, however, a striking difference in smoking habits. The percentage of non-smokers in Rønne is double the U.K. figure and 22·6% were light smokers (1–4 gm. per day) compared with 5·6% in the U.K. group. In the U.K. sample 82% smoked cigarettes alone or combined with pipes. In Bornholm only 31% of the smokers used cigarettes at all. Looked at in another way, men of this age in Rønne smoke only 780 cigarettes per head per annum compared with 3,400 smoked in U.K. groups. When comparison is made of 24 non-smokers in Rønne with 11 non-smokers in the U.K. group there is practically no difference in the frequency of respiratory symptoms and in the average ventilatory capacity. Comparison of different type of smokers shows that 2 of the physiological tests indicate that with an equal tobacco consumption those who smoke only cigarettes have more impairment of lung function than those who smoke only cigars. It is possible that the type of smoking is related to the severity of the bronchial irritation and this may be a factor of importance in the aetiology of lung cancer.

[This is an excellent example of international epidemiological enquiry on a small but valuable scale.] *A. Bradford Hill*

CARTWRIGHT, Ann, MARTIN, F. M. & THOMSON, J. G. **Efficacy of an Anti-Smoking Campaign.** *Lancet.* 1960, Feb. 6, 327–9.

The Medical Officer of Health of Edinburgh, at the cost of over £4,000, warned the public of the danger of cigarette smoking by means of (a) material inserted in the 3 widely circulated local newspapers (which also gave strong editorial support to the campaign), (b) large numbers of posters displayed on hoardings, in all omnibuses and in factories, offices, etc., (c) the distribution of 30,000 copies of a booklet, 150,000 leaflets, and a personal letter from the Medical Officer of Health to every household; (d) meetings with school teachers, secondary school children, parent-teacher groups and for the general public, and (e) by such means as a concert for young people and radio and television publicity. To measure the results, a sample of the adult population was interviewed before the campaign and a second sample after it.

There was no indication that the campaign had persuaded people to give up smoking, the forms and

amounts of tobacco consumption appeared to have remained unaltered, and just as many persons were still unwilling to believe that lung cancer is more likely to occur in smokers than in non-smokers. On the other hand there was a greater readiness to accept smoking as a possible cause of commoner and more trivial conditions, not mentioned in the campaign, *e.g.* breathlessness and cough. Before the campaign slightly under two-thirds of the informants felt that young people should not start smoking and this figure rose to just over 70% after it. About one-fifth of the adults interviewed were unaware of the campaign. It seems that campaigns of this type are unlikely to pr duce changes in behaviour except possibly in indirect long-term fashion.

[This is an excellent study in the field of pub health education and it is a pity that at least some the statistical data have not been included in it. footnote offers the tables to applicants but that is real answer to a paper which depends entirely upon statistical evidence and which the reader therefo needs to see, weigh and, perhaps, compare. And wh about the reader ten years hence?]

A. Bradford Hil

MISCELLANEOUS DISEASES

GREENWALD, I. **The History and Character of Goiter in Central America and Mexico. Its Significance for the Etiology and Prevention of the Disease.** *Texas Reports on Biol. & Med.* 1959, v. 17, No. 4, 467–88. [110 refs.]

In a previous paper (*Texas Reports on Biol. & Med.*, 1957, v. 15, 874) an account of the history of goitre in the Inca Empire was given and the present paper is concerned with the history of the disease in the home of 2 other great Indian civilizations. There is a critical examination of a large amount of the relevant literature on Mexico and Guatemala and other parts of Central America from the 16th century onwards. Goitre was probably not known and was certainly not endemic in these areas before the Spaniards came. It became general later and the earliest reports on its prevalence are of the 19th century. Throughout the region it was originally and still is more prevalent along the coast and in the lowlands that on the high plateaux. Association of goitre with cretinism and to a lesser degree with deaf mutism was noted quite early but thyrotoxicosis seems to have been and probably still is comparatively infrequent. The author states: "It is believed that the history of goiter in this region, as elsewhere, is that of an infectious disease". There is also a discussion of the value of iodized salt in prevention with stress on the dangers of the use of high concentrations of iodine (100 parts of iodine per million) since these may, in the belief of some observers, increase the number of cases of thyrotoxicosis, in certain endemic areas. *M. E. Delafield*

MUÑOZ, J. A. & ANDERSON, M. M. **Endemic Goitre in Basutoland. Report on a Survey.** *Bull. World Health Organization.* Geneva. 1959, v. 21, No. 6, 715–20, 1 fig. [18 refs.]

Endemic goitre has long been known to exist in Basutoland but there was no clear information on its prevalence until a pilot survey was conducted by team sent by the World Health Organization in 19 58 at the request of the Basutoland Government.

The report on the survey gives particulars of size, population and geography of the country and the technique used in examination. The sam studied included 13,284 individuals of both sexes a of all ages living in 7 of the 9 districts of Basutola This number of persons represented more than 2 of the total population present in the territory. It found that the endemic goitre prevalence ranged fr 30·0 to 50·7% in the 7 districts. Males and fema were equally affected in each age-group. The perce age of positives increases with age regardless of Diffuse goitre was much more frequent than nodular type.

A dietary survey showed that the salt consumpt is low (seldom more than 5 gm. of coarse salt da and that the diet consisted largely of maize, sorgh wheat, vegetables, dried beans but seldom meat, r or eggs. A table also sets out the daily *per ca* consumption of "goitrogenic" foods and vitamin in 5 rural families during every month of 1956.

Children in 43 schools were also examined and goitre incidence ranged from 0 in the Maseru E pean School to 72·7% in the Emmaus School in Mafeteng district.

The information obtained is discussed at some le with the conclusion that it would appear to be li that on the basis of the present salt consumption the fact that all the salt consumed is imported has a low iodine content "the level of iodiza should be not more than one part of potassium io per 10,000 parts of salt and not less than one par iodate per 20,000 parts of coarse salt if this se public health problem is to be overcome".

M. E. Delafie

MENTAL HEALTH

SUSSER, M. W. **A Report on the Mental Health Services of the City of Salford for the Year, 1958.** 25 pp., 3 figs.

This is an account of the mental health services provided in a progressive city of medium size before the coming into operation of the new Mental Health Act. By 1958 the ground had already been prepared and many of the underlying principles incorporated in the new legislation had, as far as practicable, been adopted. In addition to the Medical Officer of Health, Dr. J. L. BURN, and the author, the staff engaged in mental health work numbered 23 of whom 8 were employed in field work, 13 at training centres and 2 on office duties.

The work includes getting suitable patients admitted to hospital, supporting services for those remaining in the community, the provision of training centres, of a therapeutic club, and of psychotherapeutic day centres. All patients discharged from the mental hospital are notified as a routine to the service.

For the past 5 years there has been a gradual change from compulsory to voluntary admissions to mental hospitals and more care has been provided within the community. The unmet needs are more hostels, more day centres, more mental health workers with a higher standard of training and closer co-operation between the hospital and the local authority. In 1958 the adaptation of a building to provide a hostel for subnormal girls and women was almost completed and plans had been made for hostels for subnormal boys, for convalescent psychiatric patients and for old people with psychiatric problems. A day centre for chronic or convalescent male patients was opened in 1959. 2 trainee mental welfare workers have been appointed.

6 research projects are in progress to gather fundamental data and to evaluate what is being done.

The service handles about 1,200 patients a year. With regard to the mentally ill, about 40% of the 556 patients on the books of the service were referred by general practitioners but the proportion brought to notice by parents and relatives is growing and is now 20% of the total. About a quarter are over 65 years of age. In 1958 49% of the patients referred to the service were admitted to hospital. In contrast to somatic medicine where any treatment required is available freely to all, the National Health Service provides little free psychotherapy for the mentally ill.

The number of mentally defective patients on the register in 1958 was 661. During the years 1949–58, 85 patients were admitted to institutions: the discharge rate was low: but among those retained in the community the rate of discharge as they become "socially stable" is large.

An analysis is made of the time taken to pay visits. On the average each visit takes 44 minutes of which exactly half is for travelling time by public transport. The amount of supportive case work is growing and an estimate is given that if motor cars were provided the extra work which could be done would be the equivalent of an extra worker for every 2 now employed on visits. *Allen Daley*

Sanitation

The order in this section is:—**General; Water and Swimming Baths; Sewage, Trade Waste and Refuse Disposal; Housing; Infestation; Atmospheric Pollution; Port, Ship and Aviation Hygiene.**

GENERAL

ISAAC, P. C. G. [Editor.] **Report on Research carried out by the Public Health Engineering Section in the Year ended 30 June 1959.** *Univ. Durham, King's College, Dept. Civil Engineering, Bull. No. 18.* 1960, Jan., 28 pp., 10 figs. [11 refs.]

This is the 4th annual report on the research carried out by the Public Health Engineering Section of the Durham University Department of Civil Engineering. The work described was carried out by the staff and by research students.

A preliminary report is given of the results of a study of the reclamation of aluminium sulphate from the sludge derived from the coagulation of slightly alkaline peaty waters by means of sulphuric acid. The method used has given promising results which warrant further investigation.

Research on some of the newer sugar-based detergents to study their effect on the uptake of dissolved oxygen by sewage micro-organisms has continued. A large-volume manometric respirometer, which is here described, is being used in this study in addition to the chemical BOD technique.

An investigation on the production of hydrocarbons from sewage sludge using the rotating laboratory digesters and the gas-chromatographic equipment described in previous annual reports was continued.

Preliminary investigations are being made for the study of the vertical distribution of bacteria in trickling filters and the possible correlation of the bacteriological findings with changes in the chemical nature of the environment.

The Public Health Engineering Section has continued its measurements of atmospheric pollution in co-operation with the Warren Spring Laboratory of the Department of Scientific and Industrial Research and tables of the measured values of this pollution are given. *M. E. Delafield*

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

STREETER, H. W. & ROBERTSON, D. A., Jr. **Evaluation of Membrane Filter Technique for appraising Ohio River Water Quality.** *J. Amer. Water Works Ass.* 1960, Feb., v. 52, No. 2, 229–46. [11 refs.]

Membrane filter and multiple tube counts on Ohio river water were compared at 8 laboratories. Several months' experience was necessary before good agreement was obtained. Monthly medians gave better agreement between the two methods than monthly averages. Although the MF method gave lower results more frequently, greater precision was achieved. Of 3 media compared, highest results were obtained with the one-step MF Endo medium of FIFIELD and SCHAUFUS [this *Bulletin*, 1958, v. 33, 600].

E. Windle Taylor

HABS, H. & MÜLLER, H. Zur Differenzierung der coliformen Bakterien bei der Trinkwasseruntersuchung. **[The Differentiation of Coliform Bacteria isolated from Drinking Water]** *Arch. f. Hyg. u. Bakt.* 1960, Feb., v. 144, No. 1, 1–6.

The IMViC reactions used to classify coliform bacteria isolated from water were not sufficient to identify all the species of *Escherichia* [*Citrobacter*] *freundii* and *Aerobacter* [*Cloaca*] *cloacae*, types which occurred most frequently in the samples. Production of gas from glucose at 45°C., production of hydrogen sulphide and liquefaction of gelatin are also important for routine differentiation.

The scheme of classification still common in water bacteriology must be adjusted to the modern classification of Enterobacteriaceae which does not place the highest importance on lactose fermentation. On the other hand, the classification of lactose-fermenting strains requires further investigation.

E. Windle Taylor

See also p. 620, KELLY & SANDERSON, **The Effect Chlorine in Water on Enteric Viruses. II. Th Effect of Combined Chlorine on Poliomyelit and Coxsackie Viruses.**

GAILLARD, J. R. **A Bacteriological Survey of Durba Coastal and Harbour Waters.** *J. & Proc. In Sewage Purification.* 1959, Pt. 2, 243–51, 4 fig (3 on folding pl.)

The author reports a bacteriological survey coastal waters in the neighbourhood of Durb between January, 1955 and December 1958. Samp were collected from 28 sampling points along a 2 mile stretch of coastline at weekly or fortnigh intervals. The samples were examined by the tec niques of Report No. 71 [this *Bulletin*, 1939, v. 630] as used in Britain, and the results are tabulat for the different sampling points as most probable cc form counts and faecal coli counts in the range 0–1 per 100 ml. The findings are also set out diagra matically to show at a glance the proportion of samp from each sampling point that gave more than 1,C faecal coli per 100 ml.

A description is given of the local tidal and oth currents in relation to future plans for sewage dispo in the area.

In laboratory experiments the author found no go evidence of a rapid bactericidal action of sea-wa on sewage organisms. Settled sewages were dilut 1 in 1,000, 1 in 100,000 or 1 in 1,000,000 with fre coliform-free sea-water and allowed to stand periods of from a few hours up to a day, after wh the presumptive and faecal coli counts were det mined. 141 separate tests of this kind were done fr March to October, 1958. The sewages tested var considerably in strength and in degree of septic The author tabulates the proportion of samples wh still contained over 1,000 coliform organisms per ml. after this exposure to sea-water, and conclud that only if the initial dilution of sewage in sea-wa was of the order of 1 in a million would most of diluted samples contain less than 1,000 coli per 100 after 24 hours.

B. Moor

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

HOLT, H. D. **The Presence of Pathogenic Enterobacteria in Samples of Sewage collected during a Survey for Poliomyelitis Virus in England and Wales in 1951.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1960, Feb., v. 19, 29–31.

In 1951, GOFFE *et al.* [this *Bulletin*, 1960, v. 35, July] used the sewer swab technique [*ibid.*, 1949, v. 24, 187] to test the sewage of 96 communities for poliovirus in an inter-epidemic period. The present paper records the results of examining the same sewer sw for pathogenic bacteria. The sewer swabs were expressed with metal fruit presses and the fluid u for monkey inoculation. They were then returned the original containers and covered with sin strength selenite enrichment broth. Subcultures w made after 24 or 48 hours to deoxycholate citrate a containing glucose and sucrose, and also on to Wil and Blair medium.

With this technique, salmonellae were isolated fr just over 1% of the sampling points investiga

Salm. paratyphi B and *Salm. typhi-murium* were the organisms most frequently isolated. Other salmonellae cultured from the swabs included *Salm. typhi*, Tennessee, Thompson, Oregon, *enteriditis*, Montevideo, Newport, Worthington, *bovis-morbificans*, Cuba, Derby, Give, Poona, Senftenberg and St. Paul.

Shigella sonnei was isolated only from 2 sampling points. Non-haemolytic, heat-resistant strains of *Cl. welchii*, some of which were serologically identical with those associated with food poisoning, were isolated from 70 out of 115 samples from 7 communities but from none of 10 samples from an eighth.

B. Moore

WEIR, H. C. **Sewage Disposal in Low Lying Areas.** *West African Med. J.* 1960, Feb., v. 9 (n.s.), No. 1, 37–40, 2 figs.

As a proper water-borne sewage system is, for various reasons, impracticable in West Africa at the present time, the system usually adopted is that of the septic tank and soakaway which is individual to each house. This, however, is not only an expensive system but is also unsatisfactory particularly when the soil is non-porous or the subsoil water level is high. It is therefore advocated that each house should have individual drains connected to a main sewer leading to a large communal septic tank the effluent from which is then passed through a filtration system before disposal. This method is now being adopted by the Ministers of Housing in Ghana. Such a type of filtration system, devised by the author of this article, has been set up for use in Takoradi, the main seaport of Ghana, where the subsoil water level rises in places to 9 inches below the surface. This system is described shortly with some technical detail and 2 plans to illustrate the septic tank and succeeding settling and filtration chambers. The results have been satisfactory and the final effluent passing into the sea is almost completely odourless.

M. E. Delafield

ATMOSPHERIC POLLUTION

HAGE, K. D., DIEHL, C. H. H. & DUDLEY, M. G. **On Horizontal Flat-Plate Sampling of Solid Particles in the Atmosphere.** *Arch. Indust. Health.* Chicago. 1960, Feb., v. 21, No. 2, 124–31, 9 figs.

In the 5 experiments described a cloud of small glass spheres was released from a point source on a tower, and the deposition was measured at various points on 72° arcs at distances up to 800 metres downwind. In 4 experiments the mass median diameter of the particles was 108μ and the height of release was 15 metres; in the fifth the mass median diameter was 21μ and the height was 7·5 metres. For ease of counting the glass spheres were dyed with a fluorescent pigment.

The experiments were carried out over flat ground, grass- or snow-covered, and the average wind-speed up to a height of 15 metres was always less than 6 metres a second. As long as the sampling surface was at ground level, particles were deposited uniformly on it; when the surface was at a height of 3 ft., however, they tended to be at the down-wind end, and deposition was also less at the lateral edges than in the middle. With the larger particles the observed deposition up to 800 metres at ground level accounted for a very large part of the total emission.

J. McK. Ellison

MOTLEY, H. L., SMART, R. H. & LEFTWICH, C. I. **Effect of Polluted Los Angeles Air (Smog) on Lung Volume Measurements.** *J. Amer. Med. Ass.* 1959, Nov. 14, v. 171, No. 11, 1469–77, 3 figs. [17 refs.]

This paper describes experiments the aim of which was to find out whether the breathing of Los Angeles smog, in particular by those with pulmonary insufficiency, produces harmful effects measurable by pulmonary function tests.

The authors begin by outlining the nature and sources of air pollution in the Los Angeles region, and the administrative plans for dealing with emergencies due to it. The experiments which they go on to describe were carried out over a period of 3½ years in a part of the region in which pollution is quite prevalent. Of the 66 subjects, all volunteers (aged 19–71), 46 had pulmonary emphysema, and most of the rest suffered some impairment of the lung.

3 types of exposure were used, short (2–4 hours), moderate (18–20 hours), and prolonged (40–90 hours). In each experiment the subject was first exposed to highly polluted air (or, in control experiments, to clear unfiltered Los Angeles air) and then to air filtered through activated carbon, various respiratory measurements being made during each type of exposure. The results are presented graphically and also in a table. Some are mentioned very briefly, but those treated in greater detail show that in "smoggy" weather subjects with emphysema have an improved lung volume after breathing filtered air for 40 hours or longer: in particular the volume of residual air diminished. No significant changes were found in essentially normal people. Over 18–20 hours the improvement was much less, and over 2–4 hours none was detected. After 40 hours there was also significant improvement of timed vital capacity for 3 seconds and of maximal breathing capacity.

The authors conclude that Los Angeles smog aggravates existing pulmonary insufficiency. Both onset of the effects and their disappearance on breathing filtered air are delayed and only show up fully after 2 days or more.

J. McK. Ellison

PORT, SHIP AND AVIATION HYGIENE

MINISTRY OF TRANSPORT. **Report of the Committee on the Safety of Nuclear-Powered Merchant Ships** [FAULKNER, P., Chairman]. Cmnd. 958. pp. vi + 57. 1960. London: H.M. Stationery Office. [3s. 6d.]

This Report is one of absorbing interest, for in effect it presents a picture of the nuclear driven ship of the future; how a ship of this character, with great potential hazards within its structure can nevertheless take a rightful place on the waters and not in any way as a *privileged* ship (p. 25).

The terms of reference for the Committee appointed in March 1958 by the Minister of Transport were: "To advise the Minister of Transport and Civil Aviation on the safety problems arising from nuclear propulsion in merchant ships at sea and in port".

In order to deal with the safety problems it is necessary first to know the nature of the nuclear hazards and it is good to have such a forthright statement as "It can be stated categorically at the outset that it is impossible for an explosion of the atomic bomb type to occur in any nuclear reactor from any cause whatsoever".

The main hazards are, "(a) the emission of neutrons from the reactor core and the emanation of gamma rays from materials activated by neutrons" and "(b) the presence within irradiated fuel of radioactive particles, known as fission products, which the reactor is potentially capable of releasing and discharging over a wide area under certain accident conditions".

Neutrons are produced only when the reactor is in operation but the emission of gamma rays continues after shut down, decaying in intensity exponentially.

To enable the reader to get a broad appreciation of the nature of these hazards, the main features a typical installation are described (pp. 4–6).

The hazards to all working on such a ship becon clear to the reader who is then told of the extern ones. The main dangers external to the nuclear sh arise from collision, grounding, fire and explosio which might or might not be followed by sinking.

A major reactor accident far out at sea could le to the death of all people closely associated with t accident; in addition vessels in the vicinity cou suffer contamination. If such a catastrophe occurr near land the ground would become dangerous f feeding, quite apart from the loss of human life.

The greatest risk of release of fission products in the air would be that of a midships collision with vessel of comparable size (probably about 20,000 ton

With these main hazards in mind the Committ considered the principles of *Design, Construction a Survey* for nuclear merchant ships—for the next years (pp. 12–18) and *Operational Requiremer including Manning, Equipment and Safety Procedur* (pp. 19–25). Then follow shorter sections on *Dispo of Radioactive Waste* (pp. 36–37) and the *Salvage Nuclear Ships* (pp. 37–40).

Looking to the future the Committee sees problems in an international setting and its ide and proposals will doubtless get a proper hearing the International Conference which is to be held London in May–June 1960 to consider revision of t International Convention for the Safety of Life Sea, 1948. The recommendations they intend maki are given in some detail in an Appendix (pp. 48–5 together with 4 Annexes (pp. 51–57).

The Report is a noteworthy one, full of author and warrants the closest reading. *S. Rus*

Occupational Hygiene

The order in this section is:—**General; Occupational Physiology; Occupational Diseases (Dust Diseases, Poisoning, Skin Diseases, Others); Occupational Psychology; Heating, Lighting and Ventilation.**

GENERAL

MINISTRY OF POWER. SAFETY IN MINES RESEARCH ESTABLISHMENT. **Safety in Mines Research, 1958** [RAMSAY, H. T., Director]. **Thirty-Seventh Annual Report.** 71 pp., 12 figs. & 4 pls. [Numerous refs.] 1960. London: H.M. Stationery Office. [5s.]

The researches described in this report cover the whole field of safety in mines.

Various studies of explosives and blasting devices are in progress. Investigation showed that of the 8 serious gas explosions that occurred in British mines between November 1956 and the end of 1957, certai 7 and probably all 8 were caused by unsuspected c centrations of methane at the roof. Thus more inf mation about the dispersion and accumulation methane in mines is needed. This information is be provided by work on methane roof layers. M investigations are also being made of the vari aspects of the dust-explosion hazard, and on the saf of electrical circuits and appliances. A methanom has been developed, and work continues on development of methods for the rapid analysis of m gases.

In rescue work the wearing of a closed-circuit breathing apparatus tends to cause discomfort and loss of working efficiency. The wearer is affected not only by the weight of the apparatus but also by the temperature, humidity and composition of the inspired air, and by the respiratory effort needed. Current work is tending to minimize the adverse effects of the apparatus and provide cooled and reasonably dry air.

Much of the recent work on the fire hazard in mines has been concerned with the development of the foam-plug method of fighting fires. The work is now almost complete, and some specific recommendations concerning the use of the method are given in the report. Other studies deal with fire-retardant coatings on timber, and the fire-resistance of brattice cloths and conveyor belting.

Engineering and metallurgical research has ranged from fundamental work on the fatigue of metals to immediately practical work such as underground trials of improved light-weight steel roof supports.

Research into pneumoconiosis and into the measurements and suppression of respirable dust has been continued in co-operation with other bodies.

In connexion with the measurement of dust, the effect of the overlapping of dust particles in the deposits obtained by dust sampling on the accuracy of evaluation of dust samples is being investigated. A study of light-scattering and light-absorption in relation to dust measurement is in progress.

It has been held that the sampling efficiency of the thermal precipitator is influenced by the speed of the air current passing over the instrument, and that the efficiency decreases at speeds greater than 600 ft. a minute. Investigation has led to the conclusion that for practical purposes the efficiency is not affected by the speed of the ventilating current.

In experiments on the entrainment of coal dust of respirable size in a current of air it was found that dust was not raised from static deposits until the speed exceeded 800 ft. a minute, but if the deposit was disturbed mechanically there was entrainment at speeds as low as 50 ft. a minute. However, the increase in the volume of air passing along the tunnel diluted the dust so that until the speed exceeded 400 ft. a minute the concentration of dust in the air was reduced. At higher speeds the dilution was more and more offset by the increased entrainment, at speeds above 800 ft. a minute the concentration of airborne dust increased rapidly with speed. It appears that no reduction in dust concentration can be expected to result from increasing the speed above 400 ft. a minute, and higher speeds should be avoided at dusty places such as conveyor transfer points.

A dust-sampling instrument for underground use, in which the dust is sucked on to a filter paper, the sample then being evaluated by measuring its optical density, is described, and the use of the filter-paper method is discussed. A weakness of the method is that the more transparent particles, which are generally the more dangerous, are seriously under-estimated.

Thomas Bedford

ARCH. MALAD. PROFESSIONNELLES. Paris. 1959, Sept.–Oct., v. 20, No. 5, 575–672, numerous figs. 5es Journées Nationales de Médecine du Travail. Lyon, 9–10–11 octobre 1958. 2e rapport. Le bruit industriel. **[Fifth National Conference on Occupational Medicine, Lyons, 9–11 October 1958. Part 2, Industrial Noise]**

P. MOUNIER-KUHN, and J. BONNEFOY (pp. 575–585) open the discussion with a general review of the subject of noise and its effects on the auditory system. Occupational deafness has long been recognized as an entity, and they give an account of the aetiological factors, the physiological mechanisms, the histopathology of the cochlear changes, diagnosis and prognosis. They emphasize that the action of sound waves on the auditory apparatus is not yet elucidated, and that there is difficulty in distinguishing between the various causes of cochlear deafness, *viz*: age, toxicity and noise. The extent of deafness from exposure to noise is influenced by a number of factors, the intensity of noise, its frequency characteristics and the length of exposure as well as individual susceptibility. All these factors are discussed in some detail. Some mention is made of the "protective action" which, according to some authors, middle ear disease may have on the development of noise-induced deafness. They suggest that inadequate pneumatization of the mastoid process may result in a person becoming more severely deaf from exposure to noise. Of particular interest in this paper is the discussion on the fragility of that part of the basilar membrane sensitive to 4000 c/s, of the relevance to this subject of studies on the effects of ultrasonic waves on the cochlear, together with biochemical studies of the organ of Corti. Apparently, ultrasonic waves profoundly disturb the activity of diastases in this organ.

The second paper by H. NICKLÈS (pp. 585–591) gives an account of the technique to be used for measuring noise and describes in some detail the use of a French sound level meter and analysing instrument, L.R.C.E., type SSI. This portable instrument permits an analysis to be carried out in the frequency bands:—

100 to 400 c/s.
400 to 1600 c/s.
1600 to 6400 c/s.

A subjective assessment of the loudness of sound in phons can also be obtained in the ranges:—

25 to 60 phons.
60 to 80 phons, and in excess of 80 phons.

The following paper (pp. 591–598) outlines the preventive measures which can be undertaken in any situation where there is a hazard from noise. The authors, V. RAYMOND, G. SAULNIER and H. NICKLÈS, carried out a meticulous survey of the sources of noise in a boiler repair works where the level of noise varied from 76 to 96 decibels. They give a list of the machines and tools which contributed most to the overall levels. One of their conclusions is that the most effective preventive measure is suppression of noise at

source but it is also the most difficult. Some method must be found to supplant the increasing use of compressed air in industry; much more attention should be paid to the use of less noisy materials in the construction of machines. They recommend that the plans of new works or new processes should be screened by an acoustical engineer before construction.

In a further paper (pp. 598–611), G. SAULNIER elaborates on the technical problems which confront the engineer in his attempts to suppress noise at source. His thesis is illustrated by examples of processes and workshops where acoustical treatment has been applied, and it includes figures with the octave analyses before and after treatment.

M. A. TOMATIS (pp. 611–625), in a diffuse and philosophical discourse on the somatic and psychological reactions to noise, develops an ingenious theory concerning the functions of the middle ear musculature as a protective mechanism against noise, and on the possibility of reinforcing this mechanism by certain methods of training which he outlines in detail.

F. TOLOT, RÉTY, H. CHOSSEGROS and BONNEFOY (pp. 625–636) describe an environmental and audiometric study which they carried out in 40 factories, employing approximately 35,000 people, in Lyons and its suburbs. The industries are split into 3 broad groups, *viz*: metallurgical, textile and chemical, and a quarter of the factories in the first group had a level of noise above 100 decibels. The factories in the other 2 groups were fairly evenly distributed between levels of 80 to 100 decibels. Audiometric tests were carried out on 506 employees from the 3 groups, and the results are given in detail, but, briefly, 1 employee in every 9 had a severe degree of hearing loss of the type to be expected from exposure to noise.

GROGNOT and PERDRIEL (pp. 637–640) subjected 30 volunteers to a wide spectrum noise at 98 to 105 decibels for short periods, and carried out certain tests of visual function. They noted changes in regards to night vision, colour appreciation, particularly red, and the interpretation of stereoscopic responses; the evidence, however, is rather flimsy and more data need to be collected before the significance of the results can really be assessed.

The following subjects are discussed in a number of short communications; the electro-encephalographic responses to various noises, the statistical methods to be used in assessing the results of noise and audiometric surveys, the state of hearing in school leavers, the efficacy of surgery in the treatment of otosclerosis, and whether there is a need for industrial otologists.

This symposium, like most conferences on noise at the present time, contains much repetition. It emphasizes the great need for research in industry on noise and its effects on the individual and for detailed study on methods of suppression of noise at source. Perhaps, because it was held in France, it stresses the psychological aspects of the subject, and certainly these aspects must be borne in mind all the time, even in such a routine procedure as the audiometric test.

P. J. R. Challen

ALIVISATOS, G. P., ELIAKIS, C. E. & PONTIKAKIS, A. Observations sur un syndrome labyrinthique a paru subitement chez des téléphonistes. [**Observations on an Inner Ear Syndrome of Sudd Onset in Telephonists**] *Arch. Malad. Prof sionnelles.* Paris. 1960, Jan.–Feb., v. 21, Nos. 1 33–40. [13 refs.]

In this paper some of the literature on the physi disorders from which telephone operators may suf as a result of their occupation is shortly review The syndrome which is here described affected 41 of 245 female telephonists who worked in the Cent Telephone Exchange in Athens. The symptoms peared 2–3 hours after daily work began in the mon of July, August and September, 1955. There was second wave of 18 cases of the syndrome in Octob There is a table which sets out the percentage f quency of 14 symptoms of which complaint was ma These symptoms which came on suddenly inclu headache, giddiness, nausea, vomiting, constriction the chest, sleepiness, sweating, tremor, numbness a hyperaesthesia of the lower limbs, pallor, sli amnesia, pains in the neck, unsteadiness in walk and sensations of muscular and mental fatigue.

The physicians who first saw these women conside the outbreak to be one of collective hysteria. La however, 33 of the affected women were submitted expert aural examination by a special method v the findings that 21 showed increased labyrinth reflexes, 4 a diminished sensibility and 8 were norm

It is considered that the conditions of work wh are described may play a part in causing this "la rinthine syndrome" which appears so abruptly may be the result of fatigue. *M. E. Delafiel*

GAULTIER, M., FOURNIER, E. & GERVAIS, P. L'asth professionnel par allergie à la pénicilline. [**Occ pational Asthma due to Allergy to Penicil** *Arch. Malad. Professionnelles.* Paris. 1960, Ja Feb., v. 21, Nos. 1/2, 13–23. [23 refs.]

In this paper there is mention of some of the adv clinical effects which may result from penicillin ther and the authors draw attention to 2 cases of oc pational asthma which occurred in men engaged in preparation of penicillin. These cases are reported in detail with description of personal family history, the clinical examination, the results skin tests and the findings of X-ray examination of chest, of electrocardiogram examination and of monary function measurement.

There is a discussion of the difficulties of diagno of methods of therapy and of prevention. It is ho that it will be possible to find sufficiently objec methods of diagnosis and assessment to permit rational legislation in the field of occupatio respiratory allergy. *M. E. Delafie*

OCCUPATIONAL PHYSIOLOGY

LEWIS, C. E., SCHERBERGER, R. F. & MILLER, F. A. **A Study of Heat Stress in Extremely Hot Environments and the Infra-Red Reflectance of Some Potential Shielding Materials.** *Brit. J. Indust. Med.* 1960, Jan., v. 17, No. 1, 52–9, 6 figs.

The authors have evaluated industrial exposures to severe heat using the heat-stress index of BELDING and HATCH [this *Bulletin*, 1956, v. 31, 307], and they have also used the method of those authors for estimating the maximum permissible time of exposure to the severe conditions.

The heat-stress index is arrived at by calculating the rate at which the body must lose heat by evaporation in order to maintain thermal equilibrium, and expressing that rate as a percentage of the maximum rate of evaporation that is possible under the conditions of exposure. When the required and the maximum rates are equal the index is 100, and that is regarded as the maximum heat stress to which a young, healthy, acclimatized man can be subjected for 8 hours without adverse physiological effects.

In the paper environments are described for which the heat-stress indices were 524, 397 and 395. The wet-bulb temperatures were respectively 97°, 92° and 98°F., the dry-bulb temperatures were 133°, 124° and 145°F., and the globe thermometer readings were 140°, 146° and 149°F. Measurements of pulse rate, blood pressure and mouth temperature were made on 3 subjects exposed to these conditions.

It is concluded that whereas the heat-stress index is very reliable at values of less than 100, it is less reliable at values greatly in excess of 100; and it is pointed out that where the capacity for evaporative cooling approaches zero the index will approach infinity.

The limiting time of exposure to a hot environment has been defined as the time required to raise the pulse rate by 40 to 45 beats a minute and the body temperature by 2°F. The authors found that for their subjects the tolerance times agreed more closely with the earlier findings of the American Society of Heating and Ventilating Engineers and the U.S. Bureau of Mines than with the times estimated by the method of Belding and Hatch. The times estimated by this latter method were about one-third the times indicated by the earlier results, or by the authors' measurements on their 3 subjects. Thus the times estimated by the method of Belding and Hatch err on the side of safety.

In the latter part of the paper measurements are given of the relative reflectances of some materials which are of use for shielding workers against infra-red radiation. *Thomas Bedford*

WYNDHAM, C. H., STRYDOM, N. B., COOKE, H. M. & MARITZ, J. S. **The Temperature Responses of Men after Two Methods of Acclimatization.** *Internat. Ztschr. f. angewandte Physiol.* 1960, v. 18, No. 2, 112–22, 3 figs.

In the mines of the Transvaal and the Orange Free State African recruits are acclimatized by a 2-stage method. They work for 6 days in a relatively cool place and then for 6 days in a hotter one. The choice of a 6-day period for each stage is well founded, but the major part of the acclimatization is gained in 3 or 4 days. Hence it was decided to test whether it would be possible to reduce the period of acclimatization to 3 days in each of the 2 stages.

2 groups each of about 100 African mine recruits were taken at random. Both were acclimatized at the same environmental conditions and at the same rate of work. The first group underwent the usual 12-days' acclimatization, and the second worked for only 3 days in the cooler stope and 3 days in the hotter one. The wet-bulb temperatures were 87°F. in the cooler stope and 91–91·5°F. in the hot one. After acclimatization the men of both groups worked moderately hard for 2 days, under supervision similar to that during acclimatization, in a "control" stope with a wet-bulb temperature of 92°F. and a wind speed of 450 ft. a minute. The mouth temperatures of the subjects were measured.

The authors were primarily concerned with the risk of heat-stroke to new labourers working in severe heat, and from the observed mouth temperatures they computed, for each of the 2 groups, the risk of the mouth temperature reaching 105° or 103°F. after 3 hours' work. In the group acclimatized for 12 days the risk of a mouth temperature of 105°F. being reached was less than 1 in 1 million, whereas in the 6-day group it was 4 in 1,000. The risk of the mouth temperature reaching 103°F. was 3 in 1,000 for the 12-day group, and 55 in 1,000 for the 6-day group. These estimates are based on the upper 95% confidence limits.

It is clear that the abbreviated 6-day procedure is less safe than the standard 2-stage procedure taking 12 days. *Thomas Bedford*

PARMEGGIANI, L. Sodio e potassio nelle bevande e nell'alimentazione dei lavoratori ad alta temperatura. **[Sodium and Potassium in Beverage and Food of High Temperature Workers]** *Med. d. Lavoro.* 1959, Dec., v. 50, No. 12, 725–32, 1 fig. [13 refs.]

The English summary appended to the paper is as follows:—

"Normally sodium and water dietary intake occurs at the ratio 125·5 ± 26 mval/l; in high temperature workers the ratio decreases down to less than one half, and salts dietary intake becomes an important factor of water and salt balance. A study of dietary habits of Italian workers shows that sodium intake is usually of such low level (from 5·8 ± 1·7 up to 7·3 ± 2·1 g daily) to require the compensating action of kidneys during work at high temperature. Potassium dietary intake appears on the contrary to be generally adequate for workers in normal health conditions (from 2·7 ± 0·5 up to 3·7 ± 0·6 g daily). Prophylactic administration of saline beverages, containing 500 to 600 mg/l of sodium, is indicated for the prevention of symptoms due to salt deficiency in Italian workers exposed to high temperatures particularly in the hot season, when sodium elimination is increased and its dietary intake is decreased. The importance of a dietary education of the workers is particularly stressed."

OCCUPATIONAL DISEASES

MEIKLEJOHN, A. **The Origin of the Term Anthracosis.** *Brit. J. Indust. Med.* 1959. Oct., v. 16, No. 4, 324–5.

"The term 'anthracosis', meaning charcoal lung, not black or coal lung, was introduced in 1838 by Dr. Thomas Stratton following attendance at the post-mortem examination on a coal-miner."

Meiklejohn has here reprinted the original article, in which Stratton gave a description of the gross findings in an old coal-miner, and translated ἄνθρακας as charcoal [LIDDELL and SCOTT translate it as coal or charcoal]. *Charles Wilcocks*

KNAKE, Else, PETER, H. & MÜLLER-RUCHHOLTZ, W. Über die Wirkung von oligomer gelöster Kieselsäure auf Gewebekulturen. [**The Effect of Oligomer Silicic Acid on Tissue Cultures**] *Beiträge z. Silikose-Forschung.* 1959, No. 63, 35–66. [42 refs.]

The English summary appended to the paper is as follows:—

"The effect of monomer or oligomer molybdenum active silicic acid in a final concentration of 10 to 20 γ per ml. liquid nutrient upon tissue cultures of rabbit and guinea pig lung and spleen was examined. Various cultivation methods and culture media were used. The experiments were continued up to five months. The results of the investigation were perceived in the living cultures and in the coloured slices of the cultures, which had been embedded in paraffin. There was no difference between experimental and control cultures."

FINULLI, M. & GHISLANDI, E. L'acido neuraminico serico nella silicosi e nella silicotubercolosi. [**The Serum Neuraminic Acid in Silicosis and Silico-Tuberculosis**] *Med. d. Lavoro.* 1959, Nov., v. 50, No. 11, 683–7, 1 fig. [23 refs.] English summary (9 lines).

The English summary appended to the paper is as follows:—

"Serum neuraminic acid has been determined using Boehm's method in 8 normal subjects, in 50 silicotics and in 8 silico-tuberculotic patients. Such compound is about 10% of Winzler's mucoproteins, which have been found by Pernis and Calò of our Clinic to increase in simple silicosis and in silicosis associated with tuberculosis. The average of neuraminic acid was 60.2 mg.% in normal subjects, 85.0 mg.% in silicotics and 116.0 mg.% in silicotuberculotic patients. The increase of neuraminic acid in silicotics seems to be caused by the increase of mucoproteins; but in silico-tuberculotics there is certainly also an increase of the non mucoprotidic part of neuraminic acid."

WANG, Shih-Chung, Ts'AI, Liang-Wan, CHU, Shih-Y WÜ, Yi-Yuan & CHANG, Ching-Ying. **Seru Protein-Bound Hexose and Serum Protein-Bou Hexosamine in Normal and Silicotic Subjec** *Chinese Med. J.* Peking. 1959, Dec., v. 79, No. 531–7. [19 refs.]

Serum-protein-bound hexose (SPBH) and seru protein-bound hexosamine (SPBHA) are the ch constituents of the serum glycoproteins. They are al present in connective tissues, especially in their grou substance. Increased concentrations have been o served in a wide variety of diseases, particularly conditions involving connective tissues. In this pa the findings in cases of silicosis are recorded.

Sera were obtained from normal subjects and fr patients with silicosis and tuberculo-silicosis aged 1 40 years employed in a tungsten mine in Kiangsi a glass plants and potteries in Peking. SPBH was det mined by the method of MENINI (Menini *et al.*, *A Med. Scandinavica*, 1958, v. 160, 315). SPBHA by t of ELSON and MORGAN (*Biochem. J.*, 1933, v. 27, 182 in each case with a few modifications.

SPBH and SPBHA levels in silicosis were sign cantly higher than those in normal subjects and t was true even in the earliest stage of the disea Elevations were parallel with the degree of sever of the silicosis, the values being invariably higher tuberculo-silicosis than in the corresponding stage simple silicosis. Follow-up determinations of number of cases at about monthly intervals revea that both silicosis and tuberculo-silicosis patie showed a gradual increase in the concentration SPBH and SPBHA. The authors conclude that th estimations are valuable both in the early diagnc and in assessing the degree of activity of the silic process. *I. T. T. Higgin*

FAY, J. W. J., ASHFORD, J. R. & SMITH, P. H. **Int Observer Checks on Standards of Performance Evaluating Thermal Precipitator Slides.** *Brit. Applied Physics.* 1960, Mar., v. 11, No. 3, 119– 1 fig.

A detailed description of methods.

BOUHUYS, A., LINDELL, S. E. & LUNDIN, G. **Expe mental Studies on Byssinosis.** *Brit. Med.* 1960, Jan. 30, 324–6, 1 fig. [10 refs.]

It has been suggested that histamine or some ot active substance in cotton dust is responsible for dyspnoea of byssinosis. An alternative hypothesis that the symptoms are a manifestation of an alle reaction to cotton dust.

The authors studied the effect of cotton dust (p pared as an aerosol) on the lung function of 2 m who had not previously been exposed to cotton d The changes in lung function were studied by me of the nitrogen clearance method and expressed as l

clearance index (LCI) which is the amount of ventilation required to wash out nitrogen from 1 litre of lung volume down to 2% nitrogen in end-tidal gas. The LCI is increased in patients with asthma and in normal subjects after inhalation of histamine. Inhalation of cotton dust but not house dust increased the LCI in both subjects and there was good evidence that this increase was not due to the presence of histamine in the cotton dust. After inhalation of histamine the highest LCI was usually recorded immediately and this effect could be repeated on consecutive days. After inhalation of cotton dust aerosol, the LCI reached its maximum after 20 minutes but the increase in LCI could not be reproduced after a second exposure on the following day.

The authors suggest that these results and the symptoms of byssinosis might be explained by the cotton dust containing a substance capable of releasing histamine. Some further evidence was obtained from animal experiments that the cotton dust extract contained a histamine liberator. *R. S. F. Schilling*

GROSS, P., WESTRICK, Marian L. & MCNERNEY, J. M. **The Pulmonary Response to a Proteinaceous Dust.** *Arch. Indust. Health.* 1959, Dec., v. 20, No. 6, 477–88. 11 figs.

The authors exposed 10 guineapigs for varying periods up to one year to a dust containing a mixture of kaolin and the solids of boiled skimmed cow's milk. Previously, the animals had been given an intra-abdominal injection of 5 ml. of boiled skimmed cow's milk. The controls consisted of 3 groups of 30 animals each—one exposed to kaolin, one to quartz and one to ground glass dust. The average particle sizes of the dusts were of the order of 1·5 microns. The object of this experiment was to measure the effects of a dust of a high protein content and of sufficiently small particle size to reach the alveoli.

From 2 apparently unique findings, the authors suggest that the animals exposed to the milk/kaolin mixture showed a foreign protein reaction. The findings were: (1) A proliferative alveolitis distributed along scattered bronchioles. (2) The presence of isolated granulomata with eosinophilic infiltration.

The animals did not show any symptoms of sensitization and the role that allergy played in producing these lesions is not known. *R. S. F. Schilling*

SAVICEVIC, M., PETROVIC, L., STANKOVIC, M. & POLETI, D. Prophylaktische orale Verabreichung von Mosatil bei bleigefährdeten Arbeitern. II. Teil: Verabreichung mit 1- und and 3-g-Mosatil-Tabletten pro Tag. [**Prophylactic Oral Administration of Mosatil to Workers with a Lead Hazard. Part II. Use of 1 and 3 gm. Mosatil Tablets per day**] *Zent. f. Arbeitsmed. u. Arbeitsschutz.* 1959, Dec., v. 9, No. 12, 289–92, 2 figs.

In an earlier investigation [this *Bulletin*, 1959, v. 34, 1266] these authors described the results of 40-day administration of 2 gm. daily of Mosatil, a preparation of Ca2EDTA. They now compare the results of a shorter period (7 to 8 days) of oral prophylactic dosage of 1 gm. and 3 gm. respectively to 2 groups of workers, 8 in each group. All workers remained at their usual work, which involved exposure to an average concentration of fine lead oxide dust of 0·637 mgm. per cu.m.

Every second day estimations were made of lead in blood and urine, coproporphyrinuria, punctate basophilia and reticulocytosis, and all were repeated after a one-day interval following the end of the period. The reduction of urinary coproporphyrin and of lead in the blood was greater in the second group (3 gm.) than the first (1 gm.). Both groups showed a marked diminution of punctate basophilia but not a complete disappearance.

The urinary lead in both groups reached a maximum on the second day; in the first group 5 times, and in the second 6 times the original value. Thus, while the first group excreted as much lead in the urine during 8 days as would, without Mosatil, have been excreted in 33·9 days, the second group excreted the equivalent of 51·6 days.

Since these authors have previously estimated that therapeutic administration during non-exposure caused a lead excretion equal to that of only 37 days without treatment, they conclude that prophylactic administration during exposure is more effective than therapy after removal.

No variations in the blood picture, including reticulocytes, were observed nor any toxic effect on the kidneys. *Ethel Browning*

SCHIEMANN, D. Prophylaxe, Therapie und Rehabilitation bei Bleiarbeitern. [**Prophylaxis, Therapy and Rehabilitation of Lead Workers**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1960, Jan., v. 6, No. 1, 20–38, 4 figs. [16 refs.]

The author bases his prophylactic measures on a system of supervision of all lead workers; this includes clinical examination, and monthly examination of blood films for punctate basophilia. By this means the workers are divided into 3 groups—those in Stage I are "lead carriers", in Stage II lead dyscrasias, and Stage III lead toxicoses. Punctate basophilia is specific for lead poisoning only when the level reaches 6 in 50 microscopic fields. In Stage I the level is 6 to 25, in Stage II, 26 to 80, in Stage III, over 80, sometimes 230, more rarely up to 300. The stages tend to merge into each other, but the outstanding problem from the prophylactic point of view is that of deciding when Stage I is liable to develop into Stage II or III.

By keeping charts of the numbers of work people in the different stages over a number of years it is possible to distinguish a group who remain in Stage I and who are therefore regarded as a source of apparently lead-resistant individuals.

During the period 1953 to 1955, when there was an improvement in working conditions, including the use of colloid filter masks, there was practically no rise in the Stage III curve; this was attributed to the fact that all patients in Stage II were given suitable therapy, and that no person suspected of gastric disorder was employed.

Treatment in Stage I consists of bivalent iron administration until the punctate basophilia is not greater than 5 per 50 fields; this is usually within 4 weeks. Stage II necessitates removal from exposure. For colic, atropine or papaverine are given; for anorexia a pepsin mixture; for constipation, except when colic is present, castor oil followed by oil and soap enemata.

For Stage III an absence of about 6 months is advised.

The alleged prophylactic action of milk is attributed to the formation of a temporary protective layer against adsorption by the mucous membrane of the empty stomach; it is in no way an antidote to lead. Rehabilitation of the very severe cases of lead toxicosis, who can never be re-exposed, is largely a social and financial problem, referable to governmental compensation, as also is that of workers who are able to be absorbed into non-lead work with the same company but at a lower wage. When the period of compensation ends the chief problem is found with the older age-groups, who can only with difficulty adapt themselves to new work. It is suggested that men who have been lead workers for 30 to 40 years before suddenly being placed in Stage III, should be allowed to work in a department which, though not entirely lead-free, is relatively so, while being kept under strict medical control. *Ethel Browning*

FUCHS, A. Zdravotně hygienická problematika některých rtutových pracovišt. **[Sanitary and Health Problems in Persons working with Mercury]** *Českoslov. Hyg.* Prague. 1960, v. 5, No. 1, 47–55. [25 refs.]

The English summary appended to the paper is as follows:—

"It was demonstrated that in the production of distance mercury thermometers the main hazard is screwing two mercury-filled parts together and subsequent burning and welding. The relatively smallest hazard is associated with common filling and the usual careless handling of mercury where the floor is soiled with drops of mercury. To prevent these hazards it is above all necessary to do away with the above mentioned working processes involving hazards and to ensure them pneumatically. The greatest shortcomings are unsuitable surfaces (chiefly floors) in places where mercury is worked with, i.e. wooden floors from which mercury practically cannot be removed. It was demonstrated that it is possible to improve the sanitary conditions in places where mercury is worked with only by a whole series of provisions where an important part is played by doing away with lack of discipline and hygienic habits in the employees themselves. The author discusses these provisions in detail. To ascertain the degree of hazard it is further necessary to compare the sanitary conditions (mercury in the atmosphere) with the results of medical examinations (mercury content of the urine). As a result of comparisons of the mercury content of the atmosphere and mercury in the urine the author recommends to consider the value of 100 micrograms of mercury per litre of urine in collective tests as a sign of exposure to a maximum concentration of mercury in the atmosphere (0.05 mg./m³). Finally the author recapitulates the standards to which places working with mercury must comply."

VALLEE, B. L., ULMER, D. D. & WACKER, W. E. **Arsenic Toxicology and Biochemistry.** *Arch. Indust. Health.* Chicago. 1960, Feb., v. 21, No. 2, 132–51. [182 refs.]

Exposure to arsenic remains a risk inside and outside industry and this interesting account which has nearly 200 references seems to omit little. Commercial and medical uses are outlined and now the greatest danger is probably from insecticides and rodenticides and, still more, from arsine generation. Prevention lies in awareness of this.

The chemistry, pharmacology and biochemistry of the 3 main groups of important compounds, with structural formulae of organic arsenicals with a biological action, are divided from the symptoms, signs and treatment by an account of arsenic in the environment of man. This shows that he may come in contact with arsenic in a variety of unexpected ways. The relation of arsenic with nutrition in animals and men is discussed and how it happens to occur in sea, soils and atmospheric dust, in fish, wine, milk and beer, on fruits and in many food products. The account of tissue distribution includes a table of "normal" human values, shown in their variation. Arsenical sprays in agriculture are being replaced by other pesticidal agents.

Certain aspects of the metabolism and biochemistry of arsenic are now well understood and are explained. Application of this knowledge has led to a rational basis of therapy in the use of dithiols for poisoning by solid arsenic. It is disappointing that arsine toxicity could not be similarly controlled, though it has been suggested that fat-soluble mono- and di-thiols would be more likely to penetrate red blood cells and bind arsine; animals have been protected by such agents.

Among historical surveys is one discussing the association of arsenic with cancer. It is improbable that arsenic is significant in its genesis. It may be a factor in predisposition to skin cancer, but in both persons exposed and those mainly by medication. Skin and mucous-membrane irritation from arsine, though common, is controllable.

M. Patricia Fitzsimons

POLI, P. & GUYOTJEANNIN, C. Ulcérations nasales causées par des peintures à base de chromates de zinc. **[Nasal Ulcerations Caused by Paint with Zinc Chromate Base]** *Arch. Malad. Professionnelles.* Paris. 1960, Jan.–Feb., v. 21, Nos. 1–2, 50–52.

BONNELL, J. A., ROSS, J. H. & KING, E. **Renal Lesions in Experimental Cadmium Poisoning.** *Brit. Indust. Med.* 1960, Jan., v. 17, No. 1, 69–80, figs. [22 refs.]

Tubular atrophy and interstitial fibrosis of the kidney are shown in prolonged controlled experiments

to have been caused in rats by small doses of a neutral solution of Cd chloride injected intraperitoneally thrice weekly. After preliminary experiments a pilot experiment with 1 mgm. Cd per kgm. showed renal lesions from the 4th month till the last animals were killed at the 45th week. In a final 12 months' experiment, the dose was 0·75 mgm. per kgm., but this was stopped in males after 5 months and in females after 6 because of debility. However, at the end of the 7th month some of these animals were given 0·25 mgm. per kgm. until the end of the year.

Renal lesions, qualitatively similar in both pilot and final experiments, were less severe in the latter. At the year's end there was no difference in degree whether the Cd had been stopped or continued. The post-exposure progression accords with the delay in onset of human Cd poisoning which can occur years after exposure.

That the lesions were due to Cd poisoning and not to ageing or infection is suggested because, although resembling pyelonephritis, they were slightly different from it, and control litter mates were not affected. There were no inflammatory changes in the earliest lesions which, at 4 months, coincided with attainment of maximum kidney concentrations. Intensity of damage was related to dosage. In the pilot experiment, casts and numerous red blood cells were constantly found after 4 weeks but no pyelonephritis in animals killed 2–5 weeks later. No organisms were grown from kidney lesions, except in 1 of the few animals so tested. The most advanced lesions were like those in a man who died in uraemia from chronic Cd poisoning [this *Bulletin*, 1956, v. 31, 295].

Tissue concentrations in liver and kidney were of the same order as post-mortem findings in men who had been exposed to Cd fumes. Liver and pancreas peaks at 3 months fell rapidly when injections stopped. Kidney concentrations remained high. Blood cell concentrations were high from 4–6 months and spleen low until the 5th; both then fell. Other tissues showed no significant trends. [See also this *Bulletin*, 1960, v. 35, 349.] *M. Patricia Fitzsimmons*

PALMES, E. D., NELSON, N., LASKIN, S. & KUSCHNER, M. **Inhalation Toxicity of Cobalt Hydrocarbonyl.** *Amer. Indust. Hyg. Ass. J.* 1959, Dec., v. 20, No. 6, 453–68, 9 figs. [11 refs.]

Much experimental work is described in great detail and arguments are presented to show that the results obtained with this carbonyl gas could be applied to exposure to cobalt dusts. Methods are given for sampling, analysis and characterization of cobalt hydrocarbonyl, $HCo(CO)_4$ and its decomposition products. Cobalt is used as a catalyst in the oxo synthesis, and during this enclosed process the catalysts, cobalt carbonyls, are formed in the presence of CO and H. In air, $HCo(CO)_4$ decomposes so rapidly that exposure to it was in effect exposure to inorganic cobalt compounds. The composition of the particulates from the exposure chamber could have been consistent with the cobalt content of the carbonate or one of the hydrated oxides. The presence of the solid carbonyls, $[Co(CO)_4]_2$ and $[Co(CO)_3]_4$ was considered unlikely. $HCo(CO)_4$ was made by adding sulphuric acid to pyridinium cobalt carbonyl.

Acute 30-minute exposures in rats gave an LC50 of approximately 165 mgm. Co per m^3. Incidence of pulmonary oedema, calculated from the lung/body-weight ratio, was high at above 90 mgm. Co per m^3 and parallel with dilated lymph vessels. Early congestion was seen in animals killed 1 day after exposure but not 14 days later.

Repeated daily exposure for 3 months, 71 6-hour periods, of rats, guineapigs and dogs to concentrations averaging 9 mgm. Co per m^3 resulted in no chronic changes. Early deaths were due to acute effects. The lungs of those killed immediately contained nodules, aggregates of foam cells; these had disappeared in animals that were killed 3 and 6 months later; other changes were similar to control findings. A single exposure 6 months later still, to test for allergy, caused eosinophilic pneumonia in 1 of 3 guineapigs.

Chemical analyses of lungs and urine showed rapid metabolism of inhaled material. In rats, an increased haemoglobin was probably physiological: the haemopoietic response could perhaps indicate cobalt exposure in diagnosis.

[The 'oxo process is the "production of alcohols, aldehydes and other oxygenated organic compounds by passage of olefin hydrocarbon vapours over cobalt catalysts in the presence of carbon monoxide and hydrogen gases". (*Rose's Condensed Chemical Dictionary*).] *M. Patricia Fitzsimons*

KAZANTZIS, G. & BOMFORD, R. R. **Dyspepsia due to Inhalation of Carbon Tetrachloride Vapour.** *Lancet.* 1960, Feb. 13, 360–62.

A history of relief of dyspepsia during week-ends in a hospital patient prompted an environmental study of his work. He had had intermittent attacks of anorexia, abdominal discomfort, nausea and vomiting for 2 years and marked depression and irritability in the evenings for 2 months, and the attacks became worse as the week wore on. In the factory population of 14 men and 4 women, 15 of the 17 interviewed had similar symptoms, mostly during recent cold months when windows were closed. No one complained of lassitude or somnolence. No signs were found in the 16 examined; 3 had mild upper abdominal tenderness. Visual fields were normal. The hospital patient once had a raised serum-glutamic-oxalate-transaminase, the only abnormal finding. The test was normal in others and in the patient later.

About 5 litres of carbon tetrachloride—and other chemicals—were used each week for cleaning quartz crystals for electronics equipment in an unventilated factory. An uncovered beaker of CCl_4 was placed in an ultrasonic cleaning apparatus, and a vibration of about 40,000 cycles per second passed through the solution. At one of the benches, cloth soaked in CCl_4 was also used. This was stopped and the beakers were covered. Before this, atmospheric concentrations of CCl_4 near the ultrasonic apparatus were 97, 70 and 67 p.p.m., and in other places about 45. Afterwards they were 8, 9, 0 and less than 8 p.p.m. Within 1 week all workers were symptom-free and there were no recurrences. *M. Patricia Fitzsimons*

PLAA, G. L. & HINE, C. H. **The Effect of Carbon Tetrachloride on Isolated Perfused Rat Liver Function.** *Arch. Indust. Health.* Chicago. 1960, Feb., v. 21, No. 2, 114–23, 4 figs. [16 refs.]

The biochemical methods described in these experiments demonstrated that hepatotoxic effects could be recognized when CCl_4 was injected in amounts so small as not to produce histological destructive changes. In contrast, tests reported with liver homogenates and mitochondria, which have shown decreased enzymatic activity, have done so after destructive changes had appeared and the amounts administered, in relation to human toxicity, were large. Extraction from the perfusate and excretion of bromsulphthalein (BSP) by livers from normal rats were also investigated under anaerobic conditions.

Rats were subcutaneously injected with CCl_4 in doses between 120 and 960 mgm. per kgm. Livers were removed between 0·75 and 48 hours later and perfused with rat blood to which were added varying amounts of BSP and of *p*-aminobenzoic acid (PABA) and glycine. A proportion of the liver which had been ligated was removed during perfusion for histological examination. Normal livers were similarly perfused. At intervals perfusate and bile flows were measured and the perfusates sampled for BSP and *p*-aminohippuric acid (PAHA) determinations and for glucose and lactic acid levels. The biliary BSP was also determined. Normal values and indices were compared with data from the intoxicated animals.

Biliary BSP excretion in the damaged livers appeared normal and the abnormal amounts of BSP remaining in the perfusate indicated that extraction was decreased. By this sensitive BSP extraction tests dysfunction was detected 1½ hours after injection of CCl_4. Peak dysfunction occurred when microscopic alterations were minimal. Lesions were minimal 24 hours after even 480 mgm. per kgm., and after 48 hours sections again appeared normal.

Synthesis of PAHA from PABA was not consistently parallel with histological changes and was a less sensitive test for minimal damage.

Replacement of oxygen aeration by nitrogen, or nitrogen and iodoacetate, or oxygen with dinitrophenol or with fluoroacetate or with potassium cyanide indicated that normal clearance of BSP depends, directly or indirectly, upon a source of cellular energy.

M. Patricia Fitzsimons

SOUCEK, B. & VLACHOVÁ, D. **Excretion of Trichloroethylene Metabolites in Human Urine.** *Brit. J. Indust. Med.* 1960, Jan., v. 17, No. 1, 60–64, 1 fig. [26 refs.]

Quantitative relationships have been investigated in the formation and elimination of the 3 trichloroethylene (TRI) derivatives: monochloroacetic acid (MCA), trichloroacetic acid (TCA) and trichloroethanol (TCE). TRI was inhaled by 3 young men and 2 young women, who had not been in contact with it before, for 5 hours continuously in an exposure chamber; individual concentrations were at constant levels of between 500 and 850 μgm. per litre. T was repeated on 3 successive days by 1 subject anc another experiment 60 ml. of 20% glucose was admi tered intravenously and 15 units of insulin at the of the exposure. During the last 2 hours of expos TRI concentrations in expired air were determined calculate retained TRI. All urine samples for 4 c were analysed for the 3 metabolites and afterwa 24-hour samples for as long as the analytical meth permitted. Methods are described, and the litera of TRI metabolism discussed.

Table of Results
(Figures in brackets are averages)

TRI retained in mgm.	630–1,280 (915)		
,, ,, % of TRI inhaled	58–70 (64)		
	MCA	TCA	T
Total quantity excreted in mgm.	30–75 (50)	120–560 (260)	415 (5
,, ,, % of TRI inhaled	4	10–30 (19)	32 (5
Duration of excretion in hours	48–168 (112)	312–520 (387)	312 (3
Half-period of excretion:			
1st phase, in hours	15	50	
with duration, in days		5	
2nd phase, in hours		70	
with duration, in days		14	
Glucose and insulin experiment, % excreted:			
TRI alone	5	30	
,, followed by glucose and insulin	6	37	

Individual variations of TCA excretion and c fluctuation, with maximum reached about mid-day, firmed that TRI effects cannot be measured from TCA found in an arbitrary sample of urine. A metabolites appeared in the urine very soon a inhalation started, MCA, the most toxic and the quickly excreted, reaching maximum just after the of exposure, TCE shortly after and TCA within 2 hours. The average total quantity of all 3 amounte 73% of retained TRI. Glucose and insulin increase cretion by 22%, the quantity of TCE excreted on th day after exposure being 2·6 times greater, but dura of excretion was not affected. *M. Patricia Fitzsimo*

CZERNIELEWSKI, A., OLSZEWSKA, Zofia, SIKORA, Wa OMULECKI, Anastazy & TEMPSKI, J. W spr oceny odczynowości na działanie dwunitrochl benzenu wśród pracowników przemysłu barwn skiego. [**On the Evaluation of Reaction Dinitrochlorobenzene among the Dye Indu Workers**] *Med. Pracy.* 1960, v. 11, No. 1, 1 2 charts. [16 refs.]

The English summary appended to the paper i follows:—

"51 workers exposed to the action of D.N.C.B 3 to 20 years were examined. The deviation of the level and of the amount of erythrocytes was foun 42 of them. The examined workers showed the sence of professional stigma. No active patholo alterations of the skin, connected with the D.N activity was established. The functional tests of skin such as neutralization ability, the resistance t action of acids and alkalies, and patch tests were formed. The patch tests performed with 22 substa

were positive only with D.N.C.B. The epidermal tests with D.N.C.B. concentrations varying from 0.01 to 0.50% showed the differences of the sensitivity threshold of the healthy individuals not connected with production, of the clinical patients and of the workers employed in production.

"The subthreshold concentration for all tested groups amounts to 0.01% of D.N.C.B.

"With the concentration increase from 0.1% to 0.25%, the number of positive tests increases too—reaching at the concentration of 0.50%, 100% of positive tests in the cases of healthy individuals and clinical patients.

"Only 4 out of 51 examined workers did not react at all to this concentration. The intensity of reaction among the workers connected with production was smaller than in the remaining groups.

"The tendency of grouping of the positive tests with the 0.1% D.N.C.B. was established among the workers sensitive to the action of alkalies. The epidermal tests repeated after 5 months among the workers exposed to D.N.C.B. showed a decrease of intensity of reaction to 0.5% D.N.C.B. solution."

Salmowa, Jadwiga & Piotrowski, J. Próba ilościowej oceny wchłaniania nitrobenzenu w warunkach doświadczalnych. [**Attempt on the Quantitative Estimation of Nitrobenzene Resorption in Experimental Conditions**] *Med. Pracy*. 1960, v. 11, No. 1, 1–14, 7 charts. [18 refs.]

The English summary appended to the paper is as follows:—

"The experiment on the liquid nitrobenzene resorption through the skin in man were carried out and the excretion in urine of the p-aminophenol, metabolite of nitrobenzene, was studied. It was stated that the absorption velocity of nitrobenzene increases with the increase of the temperature of the skin and decreases in dependence of the duration of its contact with the skin.

"The doses of nitrobenzene absorbed through the skin being from 12 to 36 mg, the stated excretion of the p-aminophenol in urine was negligible.

"The p-aminophenol excretion was also studied in the urine of the animals (rabbits) after an intravenous injection of nitrobenzene. The characteristic picture of p-aminophenol excretion was obtained. The doses being from 10 to 100 mg/kg, the increase of the excretion efficiency from about 4 to 25 p.c. of the doses was stated.

"An experiment was made on the weekly accumulation, in 5 rabbits, the daily doses being 10 and 25 mg/kg. The experiments have shown that the nitrobenzene did not accumulate considerably in the body. It was calculated that, when the doses of nitrobenzene injected daily during a week are uniform, the increase of p-aminophenol excretion in the last day of exposure did not exceed 50% relatively to the first day of the experiment."

Von Oettingen, W. F. **The Aliphatic Acids and their Esters: Toxicity and Potential Dangers. The Saturated Monobasic Aliphatic Acids and their Esters.** *Arch. Indust. Health.* Chicago. 1960, Jan., v. 21, No. 1, 28–65, 3 figs. [Numerous refs.]

[The title gives some indication of the extent of this survey but hardly of the detail into which it goes: the points here abstracted are illustrative.]

After acetic acid, 27 esters are described in turn, some as fully as the acid—chemistry, uses, determinations in air and biological materials, irritant properties, absorption, fate, excretion, effects on systems, acute and chronic toxicity, poisoning, pathological changes, prophylaxis and treatment. Acetic acid is readily though not completely oxidized; keto bodies are intermediate metabolites. The carboxylic carbon of acetate may be utilized for the synthesis of fatty acids, and acetic acid is involved in the formation of cholesterol and in acetylation of amines. It stimulates and then depresses the nervous system, depresses the circulation and injures the kidneys, but its effect is not so much a function of the acetic radical as of its acid character.

The esters of the monovalent, bivalent and trivalent alcohols, the esters of the bivalent alcohols or glycols subdivided into mono- or diacetic acid esters or ether-esters, are discussed, and various authors' findings are collated in tables of physico-chemical and toxicological properties. It is pointed out which esters have not been completely investigated or not reported toxic to man. Useful too are the alternative names and the lists of substances for which these solvents are used.

An analysis of the first group shows, *e.g.* that boiling points increase, and vapour pressures, water solubilities and acid and alkaline hydrolysis decrease, with molecular weight—vinyl and allyl acetates falling out of line. Graphs of the alkyl acetates relate these properties to irritant and narcotic actions which increase with molecular weight. Liberation of acid by hydrolysis and solubility in water, which could be associated with irritant action, are highest, however, for the least irritant, methyl acetate: it has the lowest boiling point and highest pressure, tending to reduce its accumulation on mucous membranes. With the most irritant, butyl and amyl acetates, these 4 properties are low, favouring accumulation. The narcotic action paralleled by increasing stability on hydrolysis, is a function of the entire molecule and increases as volatility decreases. Toxicity largely depends on the narcotic action but reflex action of irritated respiratory tract nerve endings may also affect respiration. Inhalation, especially of higher homologues, may damage the lungs. Systemic effects are not always reversible, and liver and kidneys are sometimes affected.

Many esters of the second group affect the respiratory tract, liver, kidneys and heart. Glycol monoacetate and diacetate are of similar low toxicity; hydrolysis rates, if known, would be useful in interpreting nephrotoxic effects. Etherification of glycol acetate yields the more toxic methyl and ethylglycol acetates, *i.e.* the Cellosolve acetates, which are also more toxic than the corresponding 3 Carbitols, the acetic acid esters of diethylene glycol. The toxicity of triethylene glycol

acetate methyl ether is intermediate between the mono- and diethylene glycol derivatives. The propyleneglycol acetates are half as toxic as the ethylene glycol derivatives and methyl butyleneglycol acetate is more toxic than methyl ethylene glycol acetate.

The 3 glyceryl acetates, the acetins, depress the nervous and circulatory systems, injure lungs and kidneys and have some haemolytic action. Like so many esters of all groups, they have not been reported toxic in industry. *M. Patricia Fitzsimons*

VON OETTINGEN, W. F. **The Aliphatic Acids and their Esters: Toxicity and Potential Dangers. The Saturated Monobasic Acids and their Esters: Aliphatic Acids with Three to Eighteen Carbons and their Esters.** *Arch. Indust. Health.* Chicago. 1960, Feb., v. 21, No. 2, 100–113. [Numerous refs.]

This review shows what comparatively little work has been done on the 55 or so compounds surveyed. On the whole, many appear to have a low toxicity. The studies reported are in the main of feeding, injection and liver perfusion experiments. The most fully dealt with are propionic and butyric acids. Tables which show the physico-chemical properties of the alkyl propionates and butyrates include lists of substances for which these esters are used as solvents. This illustrates their extensive use and the scarcity of toxicological information. Antiseptic and fungistatic properties are a feature of the series up to pelargonic acid. Butyric acid and a few of the next highest homologues depress the nervous system and cause cardiac irregularity.

Nearly all these substances which have been investigated are ketogenic, except propionic acid, which, under the conditions described, in contrast to acetic acid, is converted to glucose and partly to glycogen. Among other exceptions are trimethyl-acetic acid, which nevertheless is only partly oxidized and is excreted as glucuronide, caproic acid which is rapidly oxidized and is not stored or converted to higher fatty acids, caprylic acid which is partly oxidized and partly fixed in the tissues, and trilaurin, the triglyceride of lauric acid which causes fat deposits containing the acid. Ascorbyl palmitates, which were synthesized as antioxidants for fats and oils, though non-toxic in chronic feeding experiments, in larger doses caused growth retardation and bladder stones. In animals on choline-free diets, ethyl laurate caused myocarditis and ethyl stearate fatty changes in the liver.

Some plasticizers mentioned appear to be non-toxic, *e.g.* triethyleneglycol diethyl butyrate or Flexol plasticizer 3GH, triethylene glycol caprylate or Plasticizer SC, and butyl stearate, and so do other esters which are touched upon, *e.g.* vinyl-2-hexanoate, triethylene glycol di-(2-ethyl-hexoate), glyceryltricaprylate, the ethyl and triglyceryl esters of pelargonic acid and its diethylene glycol ester or Plastolein X-55.

M. Patricia Fitzsimons

GILL, W. E. **Determination of NO_2 and NO in Air.** *Amer. Indust. Hyg. Ass. J.* 1960, Feb., v. 21, No. 1, 87–96, 4 figs.

WIRTSCHAFTER, Z. T. & BISCHEL, Margaret G. **R culoendothelial Response to Pentane. A** *Indust Health.* Chicago. 1960, Feb., v. 21, No 152–9, 8 figs.

Microphotographs of imprints of tissues, removed serial autopsies from rats after subcutaneous injec of 0·4 ml. per kgm. of pentane and from normal show differences in cellular morphology. The impr ing technique consists in lightly touching the slide the tissue, held in forceps, in a straight up-and-d movement across a series of slides, in such a man that 1 layer of cells adheres and a series of impr from different areas of each organ are seen on 1 s The technique is being used for benzene and a t shows similarities and differences in the femur mar response to pentane and carbon tetrachloride. Bl counts after pentane showed moderate neutrop and monocytosis in 24 hours and these changes persi until the last of the 3 weeks' serial observations.

Pentane imprints showed that the reticuloendoth (RE) response persisted in marrow, spleen and ly nodes. In the marrow, cells of RE origin incre 1 hour after injection, reached a peak in 1 week remained twice as many as in the normal mean co Apart from a few early atypical cells, there were morphological changes. In the spleen, plasmac increased only for 48 hours, and cells of RE or began to increase in 30 minutes and totalled 1 times the normal value during the experiment. Ly nodes showed a marked increase of plasmacytes, plasmacytes and mature macrophages, with a comitant increase of lymph type RE cells. The was unaffected and so, except for a few early cha was the thymus. *M. Patricia Fitzsimo*

HEROLD, K. & SASSE, K. Gefährliche Gase bei Ka sationsarbeiten. **[Dangerous Gases in Sewe Work]** *Ztschr. f. ärztl. Fortbildung.* 1960, Fe v. 54, No. 3, 156–8.

In this paper the author describes the circumst of several accidents, some fatal, which happene sewermen working in an enclosed space and were to their exposure to benzine, a high concentratio carbon dioxide, sulphuretted hydrogen or hydroc acid. A number of accidents due to other gases as coal gas, methane and acetylene have been reco in the literature quoted.

There is a discussion of the variety of diff causes, some of neglect or carelessness, which may b about dangerous concentrations of these gases. description is given of the legal enactments for co which are in force in Germany. Stress is laid on importance of adequate instruction of the worke safety precautions and also in first-aid measure cases of accidents. *M. E. Delafie*

BARDODĚJ, Z. Hodnota a použití expozičních t IX. Fenolový test. **[Value and Use of Expo Tests. IX. Phenol Test]** *Československ. Hyg.* Pr 1960, v. 5, No. 1, 39–46, 7 graphs. [17 refs.]

The English summary appended to the paper follows:—

"The maximum permissible concentration of benzene in the atmosphere, valid in Czechoslovakia is 0.05 mg./l. which is considered safe and to which the following levels in the urine correspond:

"a) The phenol concentration in the total amount of urine excreted per day should not exceed 50 mg./l. and the percentage of inorganic sulphates from the total amount of sulphates should not be less than 80.

"b) The phenol concentration in urine at the end of the working shift must not exceed 100 mg./l. and the percentage of inorganic sulphates must not drop below 75.

"In the maximal permissible atmospheric concentration of phenol which is 0.02 mg./l. and which is considered safe, the phenol concentration of the urine during the second half of the working shift must not exceed 70 mg./l.

"For control examinations of employees working with benzene, phenol and cresol the author recommends urine analyses at the end of the shift. The phenol test is more suitable than the test of the sulphate ratio because it is selective, more sensitive and less time consuming. The sulphate test is, however, a suitable supplement of the phenol test because it is less dependent on the diuresis.

"When carrying out the phenol test the author recommends to separate the phenol from the urine by steam distillation and to estimate photometrically a distillate with 4-amino-antipyrine."

WATROUS, R. M. & OLSEN, R. T. **Diethylstilbestrol Absorption in Industry: a Test for Early Detection as an Aid in Prevention.** *Amer. Indust. Hyg. Ass. J.* 1959, Dec., v. 20, No. 6, 469–72, 3 figs. [14 refs.]

This bioassay procedure appears valuable for the control of this problem which a review of the literature shows still to be widespread [this *Bulletin*, 1945, v. 20, 209], especially since the use of stilboestrol in animal husbandry has increased the number of people at risk.

Groups of 10 immature female mice, weighing 8–10 gm., are injected orally each day for 3 days with 0·2 ml. of diethylstilboestrol standard or of urine passed on the latter mornings of the week by stilboestrol operators. On the 4th day the mice are killed and the uteri, stripped of appendages, are weighed in groups of 10, after pressure between filter papers to remove intra-uterine fluid. From control mice the average uterus weight is about 8 mgm.; from mice receiving a standard of 0·06 μgm. stilboestrol per ml. it is 16 mgm., and with a standard of 0·18 μgm. per ml. it is 31 mgm.

Unexposed workers excreted oestrogens below the threshold of the test, 0·02 μgm. per ml. of urine. Exposed and imperfectly protected workers showed values ranging from 0·06 to 0·55 μgm. per ml. Weekly urine monitoring for 1–2 years, illustrated by graphs, showed absorption before signs; tenderness of nipples or subareolar induration appeared 1–2 weeks after excretion reached or exceeded 0·1 μgm. per ml.

Intermediate products when tested showed oestrogen activities only 1/320–1/1000 of that of stilboestrol; no special precautions were taken in this part of the process and the workers there had negative tests and no symptoms. In the final synthesis of diethylstilboestrol, in spite of stringent precautions, similar though even more elaborate than those previously recommended, men when first assigned to the work showed increased excretion within 1–2 weeks. A supervisor trained in handling sterile powders found small loopholes, but the problem could not be said to be more than barely solved by all the methods which could be devised; these are described. *M. Patricia Fitzsimons*

KANAGARATNAM, K., BOON, W. H. & HOH, T. K. **Parathion Poisoning from Contaminated Barley.** *Lancet.* 1960, Mar. 5, 538–42.

With the increasing use of toxic organic phosphate compounds as insecticides in agriculture a number of cases and outbreaks of poisoning in man have been reported [this *Bulletin*, 1959, v. 34, 1205].

An explosive outbreak of parathion poisoning occurred in Singapore in September 1959. It became manifest on September 6th when, between 4 p.m. and midnight, 13 children of whom 8 were in coma, 1 child who was found to be dead and 1 adult were admitted to the General Hospital. The total of persons in whom parathion poisoning was diagnosed on the 6th, 7th and 8th of September was 38—35 children, of whom 9 died, and 3 adults. There is a good account of the clinical picture with some case records. Treatment was by atropine which was in general very effective and by supportive measures.

The common factor in all patients was the consumption of boiled barley. Immediate steps of control were taken which included making "barley-poisoning" notifiable and wide publicity by radio, loudspeaker vans and in the newspapers.

Careful and intense investigation was made of barley stocks in retailers' and wholesalers' premises and many chemical analyses were carried out. The general conclusion reached was that some bags of loose pearl barley imported from Western Europe in August by a cargo boat had in some unknown way become contaminated in transit by parathion which is not available in Singapore. Imports of fresh, loose barley were stopped for 3 months while local stocks were checked.

There is a discussion of the toxicology of organic phosphate compounds with mention of the value in treatment of the cholinesterase reactivators pyridine-2-aldoxime methiodide (P2-AM) and the methane sulphonate (P2-S) which drugs were not available in Singapore at the time of the outbreak. *M. E. Delafield*

BROWNING, Ethel [M.D.]. **Harmful Effects of Ionising Radiations.** With a foreword by W. V. MAYNEFORD, C.B.E., D.Sc., F.I.P. pp. xii + 158, illustrated. 1959. Amsterdam. London. New York. Princeton: Elsevier Publishing Co. [15s.]

Dr. Browning's excellent book is a survey of a big subject. She states that "These problems are envisaged primarily from the point of view of industrial medical officers, safety officers and workers engaged in this

field of industry, but the general population cannot now be separated from the industrial with regard to the possible biological effects of atmospheric radioactive contamination . . .".

The first 64 pages are devoted to the physical and general aspects of ionizing radiations, with special reference to their measurement and to the various means now adopted in industry to avoid the hazards to man of undue exposure to them. During recent years these means have been explored in great detail with the welcome result that with faithful observance of regulations which provide for their safety, employees may, in the great majority of industrial processes, feel a sense of security. Accidents will happen, that much is admitted, but even so, those occasions by prompt action, are greatly diminished in their potential harm.

The remaining pages (94) are devoted to *Biological hazards of ionizing radiations* together with a good working Index.

This part of the book is divided into four sections, the main subject-matter being as follows:—

(1) Acute and subacute effects; (2) Chronic and delayed effects; (3) Leukaemia; (4) Genetics.

It would be difficult to find any important damaging effect of the ionizing radiations which is not dealt with in these pages. There is a scientific detachment in the writing; this does not prevent the author from entering a controversial field such as, for instance, the production of leukaemia by means of indirect radiation; the facts are given and the reader may come to his own conclusion.

The book closes with *Genetics*. Since the first observations of Muller in 1927 upon mutations induced by X-rays, biologists became aware of a fact having great significance for the human race and this has grown greater over the years, for our background radiation from which we cannot protect ourselves, is increasing. This chapter is beautifully put together and is a fitting end to a book which has earned a very wide circle of readers. *S. Russ*

MINISTRY OF LABOUR. **Factories Acts, 1937 and 1948. Factories (Ionising Radiations). Special Regulations. Second Preliminary Draft of Regulations.** 20 pp. 1960. London: H.M. Stationery Office. [1s. 3d.]

Those who make use of the preliminary draft of the Special Regulations issued by the Ministry of Labour in 1957 [this *Bulletin*, 1957, v. 32, 1073] will do well to put them aside because the present issue contains a large number of changes; these have been made because of comments by the users and because of revised recommendations by the International Commission on Radiological Protection, issued in the interim. The more important changes made are listed in a Preface of 4 pages; in addition to the actual changes made in the text there is one new regulation; Regulation 28. The wording of this new Regulation begins thus: "Where any person ceases to be employed by an employer by whom he has been employed in the processes that employer shall, if he knows the whereabout of that person, forthwith supply him with a copy of the record concerning him in the Health Register . . ."

The form of expression seems cumbersome, thou the intention is clear. Clarity is not a claim that co be made for the following, taken from p. 20, line "Without prejudice to the provisions of the preced sub-paragraph, the number of rads in the total cur lative dose received by any person employed in processes at or near the surface of the eyes (exclus of beta radiation not exceeding 2·5 MeV) or fr X-rays or gamma rays shall not at any time exceed t times the number of years from the first day of Janu of the year in which he attained the age of eighteen."

Observations are invited on this revised Prelimin Draft. These should be sent to the Ministry of Labo 8 St. James's Square, S.W.1., by the 15th April, 1960. *S. Rus*

MALKINSON, F. D. **Percutaneous Absorption of To Substances in Industry.** *Arch. Indust. Hea* Chicago. 1960, Feb., v. 21, No. 2, 87–99. [refs.]

A useful concise survey of the principles govern skin absorption deals with numerous poisonous che cals and has helpful references.

Diagrammatic cross sections show the 2 pathwa the trans-epidermal and the trans-appendageal— latter, the relatively permeable pilo-sebaceous appara Passage through the former of water, electrolytes water-soluble non-dissociable substances is determi by electric forces of a superficial barrier with a fibri network between the upper stratum corneum and stratum malpighii. Once passed, there is seemingly impediment to diffusion through the remaining dermal cells and into the corium and circulation, tho for some materials the basement membrane form second barrier. Penetrability of lipid-soluble substan is dependent on a sterol-phosphatide framework wi cell membranes. These substances are rapidly absorb especially if also moderately soluble in water. G enter by both routes and more easily if dissolved skin moisture which if increased, by whatever ca facilitates penetration of all absorbable chemic Transfollicular absorption by-passes the barrier, spread into the corium may be followed by epider penetration from below as far as the barrier.

Organic phosphorus and chlorinated hydrocar insecticides, carbon tetrachloride, aromatic amines aniline, nicotine, dinitrophenol and hydrogen cya are among examples whose effects are described toge with methods of protection. Arguments for and aga skin absorption contributing to the effects of hydrc sulphide and trinitrotoluene are given. Decontam tion of radioactive substances brings out the ge danger of abrasions, pre-operative shaving and the of wetting or complexing agents: these may incr absorption.

Percutaneous toxicity tests should take into acc the physiology of normal and of injured, inflamed s lipid and water solubility, vaporization, irritant ef the rate and extent of absorption and, in industrial augmenting factors such as those mentioned and heat, solvents and the possibility of dusts accumula on hair. *M. Patricia Fitzsimo*

MARCUSSEN, P. V. **Ecological Considerations on Nickel Dermatitis.** *Brit. J. Indust. Med.* 1960, Jan., v. 17, No. 1, 65–8, 2 figs. [42 refs.]

An analysis of the records of patients who had attended the Finsen Institute Department of Dermatology, Copenhagen, and who had true nickel dermatitis, follows a review of the literature showing that the condition has increased among the general population. Of 621 patients seen between 1936 and 1955, only 4% had been sensitized in the nickel-plating industry, where the risk is recognized and controlled. An impression that a larger proportion than this had dermatoses caused or aggravated by occupation was strengthened. 272 patients with dermatitis of the hands were classified into 12 occupational groups and the remainder were then assigned to the same groups. A disproportionately large number with hands affected were found in each of 8 groups, *e.g.* hairdressers, nickel platers, metal or tool handlers, tailors, etc. In these, the exposed occupations, there were 163 cases of dermatitis of the hands among 192 cases of nickel dermatitis, but in 88 the hand eruption was secondary, sensitization having occurred elsewhere on the skin from jewellery, spectacles, watches and particularly suspenders. In the less exposed groups, cleaners, office workers, housewives and others, the hands were affected in 109 of the 429 patients, and the eruption on the hands was secondary in 70.

In the whole series, only 4% could be attributed to nickel-plating, while in 9·5% the dermatitis had developed in other occupations and in 86·5% it was caused by articles in everyday use. Of the last, 14% were later exposed to nickel in their work and developed dermatitis of the hands, and in 45% of cases of occupational dermatitis of the hands nickel-plated suspenders were responsible. Preventive measures are necessary for the community and for artisans and tradesmen rather than for workers in the large industries.

M. Patricia Fitzsimons

CALNAN, C. D. **Cement Dermatitis.** *J. Occup. Med.* Chicago. 1960, Jan., v. 2, No. 1, 15–22. [50 refs.]

This condition, infrequent during cement manufacture but frequent during use, has an association with chromate sensitivity, sometimes explained as an allergic hypersensitivity to hexavalent chromium salts and sometimes said to be the principal cause of the dermatitis. Reviewing the history of the disease, the literature and patch-testing and the occupations and varied clinical picture of patients in his London hospital and his experimental work, the author considers that cement dermatitis is not chromate dermatitis but a primary irritant dermatitis complicated, in most instances, by a secondary contact sensitivity to hexavalent chromate.

Manufacture of Portland cement by the wet process is outlined; ash from the coal fuel is mixed with cement clinker. Soluble chromate was found, in varying amounts, in most of 24 samples of British cements. Tables of determinations of chromate and total chromium, both expressed as μgm. potassium dichromate %, are given for raw materials, intermediary stages, finished cements and experimental materials. Chromium, but no chromate, was found in the clay, chalk, slurry and gypsum, the starting materials. Secondary sources of chrome compounds were the refractory-brick kiln-linings, coal ash and, sometimes, chrome steel in the grinding mills. Chromate was found in clinker, ash and cement in similar amounts, more than could be accounted for by the 5% ash in the cement. Much of the chromate in the cement originated in the kiln by oxidation of trivalent chromium in the slurry. This process was duplicated by laboratory tests; after burning, slurry, chalk and clay contained hexavalent chromate.

Patients who were patch-test positive to 0·1% chromate solution, about two-thirds of the cases of cement dermatitis, also responded, with no disparity, to 0·001% intradermally. Trivalent salts gave no allergic reactions. The nature of cement dermatitis is discussed: the physical qualities of cement are sufficient to irritate skin without invoking any other mechanism beyond a superimposed dermatitis venanata from chromate.

M. Patricia Fitzsimons

HODGSON, G. **The Tolerance of the Skin to Lubricating and Cutting Oils.** *J. Occup. Med.* Chicago. 1960, Jan., v. 2, No. 1, 32–8. [13 refs.]

Intact skin in normal and eczematous subjects was tested with several oils in 4 main experiments, in Cardiff, Wales. Results of prophetic 24-hour patch tests with challenge 2 weeks later, and of repeated insult tests on alternate days for 1 month with a 48-hour challenge 2–3 weeks later, coincided with accepted ideas.

Crude petroleum residues or the ordinary distillation cut are used in preparing engine liquid oils, cutting oils and solid greases. Engine lubricants contain differing proportions of thin spindle and medium and thick cylinder oils, with antioxidant, detergent and anti-rust additives. Additives may render suspect the good skin-tolerance reputation of the lubricating fraction of petroleum. Soluble (emulsion suds) cutting oils are mixtures of spindle oil and sulphonates, with added disinfectants, oxidation inhibitors, antiseptics and water softeners or hardeners. Insoluable cutting oils include the extreme pressure (EP) sulphurized, chlorinated or sulphochlorinated oils. Cutting oils are a frequent cause of dermatitis—emulsion oils because of soap-like and oil solvent effects, high *p*H, rancidity and additives, and insoluble oils by blocking hair follicles. Furthermore, after use metallic swarf causes mechanical injury and overheating may produce irritant compounds.

Lubricants tested were: a turbine naphthenic spindle oil and a transformer refined spindle oil, each tested alone and with added antioxidant, 0·1% phenyl-α-naphthylamine, and the latter mixtures after oxidation, which simulated use. 3 EP oils containing a 0·1% copper-staining inhibitor, were tested before and after machining, and 3 soluble cutting oils containing special soaps and cresylic acid or xylenols. Finally, crude oil residue scraped from the emptied cargo tank of a petroleum tanker was tested.

Normal skins were unaffected except that continued exposure to soluble oils and to some sulphochlorinated oils contaminated with metals caused irritant reactions. Intolerance to all, except the tanker oil, was demonstrated in 30–36% of eczematous subjects. Use did not influence the irritancy of lubricants, but increased the irritant effects of EP oils. No sensitization was recorded to the 2 additives which were tested separately. On normal skins there was little difference between t number of positive reactions from each type of pa test. During the repeated insults in eczematous subje more reactions occurred than on subsequent challen and than on normal skins. [There is a valuable acco of the composition, purposes and effects of oils a additives and of deductions from the results in t control of dermatitis.] *M. Patricia Fitzsimons*

Food and Nutrition

The order in this section is:—**General; Foodstuffs; Food Poisoning.**

FOODSTUFFS

Composition and Bacteriological Control

CLIFFORD, P. A., BASSEN, J. L. & MILLS, P. A. **Chlorinated Organic Pesticide Residues in Fluid Milk.** *Pub. Health Rep.* Wash. 1959, Dec., v. 74, No. 12, 1109–14.

During August to November 1958 the U.S. Food and Drug Administration conducted a nationwide survey of antibiotic and pesticide residues in raw fluid milk. The findings on antibiotic residues have been published (*Antibiotics & Chemotherapy,* New York, 1959, v. 9, 393).

The present paper contains description of the plan, objectives and results of a survey of 936 raw milk samples which were tested for residues of chlorinated organic pesticides. It was the object of the survey to determine the incidence, range and source of these residues; and also to test the value of the analytical procedure of paper chromatography. This method was used for "residues of DDT, DDE, DDD, lindane, BHC, dieldrin, chlordane, methoxychlor, toxaphene, and heptachlor": and in 23 (2·5%) of the 936 milk samples substantial residues were indicated (the definition of "substantial" was fixed at 0·1 p.p.m. or more). 17 of the samples with substantial residues were then further examined by the appropriate more exact quantitat methods, and 4 of these were found to be false po tives. 49 samples which were negative by pa chromatography when analysed by the exact metho gave no positive results.

There are several tables of results which include findings of fly bioassay of 168 samples in comparis with those obtained by chromatography.

Among the general findings of the survey are: "DDT was the most notorious offender", (2) "th has been a definite improvement in the milk resio picture" since the survey of 1955, (3) "paper ch matography is a useful procedure in detecting s stantial residues", (4) fly bioassay yielded a h percentage of toxic reactions "due to the fact that bioassay reflects the sum of all residues toxic to housefly" and (5) the source of contamination of milk was determined in only 3 of 8 milks with h residues which were investigated—feeding of c silage contaminated with DDT in 1 instance and ca less spraying of barns with a concentrated DDT solut in 2 cases. *M. E. Delafiel*

FOOD POISONING

MEDCOF, J. C. **Shellfish Poisoning—Another North American Ghost.** *Canadian Med. Ass. J.* 1960, Jan. 9, v. 82, No. 2, 87–90, 4 figs.

This paper was presented at a meeting of the New Brunswick and Prince Edward Island Branch of the Canadian Public Health Association in 1959. Probably the first published account of paralytic shellfish poisoning in Canada was written in 1793. It described an outbreak among the crews of 2 small-boat parties during Captain George Vancouver's voyage of exploration on the coast of British Columbia. This form of shellfish poisoning is known also in 2 districts on the east coast of Canada—the estuary of the St. Lawre and the Bay of Fundy. A map gives the distr where poisonings have occurred, some of which c back to the period 1800–1810. There is an acco of some of these outbreaks and a review of the pres methods of control of the commercial harvesting clams (*Mya*) and of the warnings put up on beac to protect picnickers and others from digging cla during the seasons when danger exists. These warni have been disregarded with regrettable results as in outbreak in 1957.

There is a discussion on how the system of con might be strengthened. There is some evidence

"in summers following cold winters the poison conditions are worse than in summers following mild winters" and in conjunction with this it has been observed that in the Bay of Fundy the average water temperatures have been decreasing. On these facts it might be possible to devise a longer-range method of forecasting the danger period. The author expresses his view that the present elaborate system of forecasting by determining the amount of toxin in the shellfish might be simplified by biological studies to obtain more knowledge of the dinoflagellate, *Gonyaulax tamarensis* from which the shellfish derive the toxin.

M. E. Delafield

Mycoses and Mycology

The order of diseases and fungi in this section is:—**General; Dermatophytes; Blastomyces; Histoplasma; Sporotrichum, Phialophora; Candida, Cryptococcus; Actinomyces, Nocardia; Aspergillus; Others.**

Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN.

BEARE, M. & MACKENZIE, D. **Griseofulvin in Treatment of Infections of Scalp due to** *Microsporum canis*. *Brit. Med. J.* 1959, Nov. 28, 1137–40, 1 diagram.

"In our experience griseofulvin is non-toxic to children in a dose of 0.25 g. three times daily for periods of up to 10 weeks.

"Fungal invasion of hair is stopped abruptly soon after the drug is given and new areas of infection do not appear. Debris, probably intrafollicular, remains infected and the organism can be recovered readily for long periods (up to 14 weeks) after treatment has started.

"Wood's-light fluorescence usually disappears in one to six weeks (average 3 weeks). With *M. canis* infections, fluorescent tips are only exceptionally found.

"In one rather unusual case in the series, fluorescence was observed eight weeks after treatment had started; after the second week this fluorescence appeared at various distances from the surface of the scalp; positive cultures were obtained up to 12 weeks after the initiation of treatment, and microscopical examination often revealed a well-established infection in a non-fluorescent portion of hair.

"Future studies should be directed towards a method for the removal of infected debris. Such methods might include washing, scrubbing, and/or shaving the affected areas, and the application of local fungicides. It is already apparent that, though griseofulvin is a most remarkable advance in antibiotic therapy, it is insufficient in itself to cure scalp ringworm (at least that due to *M. canis*) within a reasonably short period."

[A valuable analysis based on the results of treatment in 19 cases.]

BARLOW, A. J. E., CHATTAWAY, F. W., HARGREAVES, G. K. & LA TOUCHE, C. J. **Griseofulvin in Treatment of Persistent Fungal Infections of the Skin.** *Brit. Med. J.* 1959, Nov. 28, 1141–3.

"Thirty-four patients with fungal infections of the skin have been treated with oral griseofulvin in a dosage of 1–2 g. daily.

"Two children with candidiasis and one man with tinea versicolor showed no improvement.

"Two patients infected with *Trichophyton verrucosum* derived no significant benefit.

"Infection by *T. mentagrophytes* in one patient cleared after four weeks' treatment.

"Two cases of *T. rubrum* infection of the smooth skin were treated for three weeks; one cleared completely and the other improved.

"Twenty-six patients with long-standing *T. rubrum* infection with nail involvement were treated for periods of 3–20 weeks. The majority improved but in only one instance was the infection eradicated.

"Toxic reactions are recorded and possible reasons for the wide variations in clinical response discussed."

BLANK, H., SMITH, J. G., Jr., ROTH, F. J., Jr. & ZAIAS, N. **Griseofulvin for the Systemic Treatment of Dermatomycoses.** *J. Amer. Med. Ass.* 1959, Dec. 19, v. 171, No. 16, 2168–73, 7 figs. [16 refs.]

The authors treated 200 patients presenting with lesions in various sites (numbering 311) with orally administered griseofulvin.

All lesions of the smooth skin, nails, soles, palms and scalp responded favourably to treatment with a dosage of 0·5 gm. to 1·0 gm. In the case of lesions of the glabrous skin it was found that therapy over a period of 3 weeks was adequate. In the case of lesions of the palms and soles, treatment was prolonged to from 4 to 8 weeks. For finger-nails and for toe-nails 4-months' treatment and 6-months' treatment respectively were required.

In the case of scalp lesions 3-weeks' treatment for fluorescent types and 6-weeks' treatment for non-fluorescent types were required.

Pruritus was relieved in 2 to 6 days in lesions of the palms and soles, while vesiculation and scaling ceased within 2 to 6 weeks. Also cultures became negative in from 2 to 6 weeks.

No serious side-effects resulted from treatment in all these cases.

C. J. La Touche

LAMPEN, J. O. & ARNOW, P. **Significance of Nystatin Uptake for its Antifungal Action.** *Proc. Soc. Exper. Biol. & Med.* 1959, Aug.–Sept., v. 101, No. 4, 792–7, 1 fig. [14 refs.]

This is an extension of the authors' previous work [LAMPEN *et al.*, this *Bulletin*, 1960, v. 35, 384] showing that the uptake of nystatin by sensitive organisms exceeds that of resistant ones. They first determined the time required for different concentrations of nystatin to arrest the respiration of *Saccharomyces cerevisiae* and the amount of antibiotic absorbed. Studies were then made of 4 *Candida* spp. (*C. guilliermondii, C. parakrusei, C. tropicalis* and *C. stellatoidea*) each being represented by the original sensitive culture and a more resistant variant. The latter absorbed less nystatin, but the differences in the amounts absorbed did not correspond to degrees of difference in resistance, suggesting that reduced uptake is not the only basis of resistance. There was closer correspondence between degree of resistance and the concentration of nystatin required to inhibit respiration. Serum albumin, which protects *S. cerevisiae* against the action of nystatin, was shown to reduce absorption of the antibiotic. The protective action of some other substances was also studied. The methyl ester and N-acetyl derivatives of nystatin, which are not inhibitory, were found not to be significantly absorbed. *L. P. Garrod*

GÖTZ, H. Zur Morphologie der Pilzelemente im Stratum corneum bei Tinea (Epidermophytia) pedis, manus et inguinalis. [**Morphology of the Fungal Element in the Stratum Corneum in Tinea of the Foot, Hand and Inguinal Region**] *Mycopathologia.* The Hague. 1960, Feb. 25, v. 12, No. 2, 124–40, 16 figs.

EVRON-MAOZ, R. & RAUBITSCHEK, F. **The Morphology of the Pseudoparasitic Phase of Some Dermatophytes.** *Mycopathologia.* The Hague. 1960, Feb. 25, v. 12, No. 2, 111–23, 15 figs.

SCHWARTZMAN, R. M., FUSARO, R. M. & ORKIN, M. **Transmission of North American Blastomycosis. Possible Case of Transmission from Dog to Human.** *J. Amer. Med. Ass.* 1959, Dec. 19, v. 171, No. 16, 2185–9, 6 figs.

In this article North American blastomycosis is described in a dog and a man living in a small community. Although this dog did not belong to the man it was owned by some of his friends.

In April 1959 the dog, which had a history of febrile debilitating disease with cough and shedding of hair for a month before examination, presented with a purulent ulcer "3 cm. in diameter with an erythematous granular surface and rolled borders" on the right lateral tarsus, as well as 3 punched-out ulcers on the right flank. X-rays did not reveal any involvement of the bones but only soft tissue swelling of the tarsal area. A biopsy of this area showed on microscopical examination numerous double-contoured bodies (Schi positive), and a culture of pus from this lesion yield *Blastomyces dermatitidis.* X-rays of the lungs reveal bronchiectasis of the diaphragmatic lobes.

The disease ran a rapid course and shortly af admission the dog's life was humanely terminate Autopsy revealed, among other features, foci of infe tion in the lungs in the form of confluent greyish whi " relatively firm nodules (2 to 4 mm. in diameter) . beneath the pleura and within the parenchyma Cerebral lesions were also present.

In June 1958 a 52-year-old man consulted doctor concerning a swelling of his right knee which had injured 8 days previously. Antibiotics we administered without effect. Chest X-rays revealed mass in the right hilus and also cardiomegaly.

He was admitted to hospital where he became rapi worse and died on July 14th 1958 in spite of dilig therapy.

At autopsy "numerous individual nodules, 7 to mm. in diameter, were scattered over most of the lu parenchyma".

Histological examination revealed numerous "doub contoured" cells. Unfortunately, cultures were negat for fungi.

An increasing number of case records of this dise in dogs is mounting evidence for the possibility t these animals when so infected might be in turn source of infection for man, a possibility which strongly emphasized in this dual case record of disease in which its incidence in the dog prece that in the man by only 3 months.

C. J. La Touch

CONRAD, F. G., SASLAW, S. & ATWELL, R. J. **T Protean Manifestations of Histoplasmosis Illustrated in Twenty-Three Cases.** *Arch. Inte Med.* 1959, Nov., v. 104, No. 5, 692–709, 14 f [38 refs.]

This clinical account of a number of cases of hi plasmosis not only illustrates the variability of clinical manifestations of this disease but also emp sizes the necessity for being alert to the possibility its being associated with some other prima established disease.

In addition to various clinical examinations a num of tests and investigations were carried out in each c These include: blood counts; serological tests such the histoplasmin, collodion agglutination and com ment-fixation tests; culture of sputum, and, in number of cases, histological examination of bio material. X-ray films were exposed in all cases, the findings obtained thereby were not sufficie specific to be of diagnostic significance.

Of the 23 patients who were fully investigated it possible in only 11 to culture *Histoplasma capsulat* in 2 others this organism was demonstrated mi scopically but cultures were negative.

Diagnosis was established on the basis of serolog tests alone in 10 cases; on the basis of culture serology in 11 cases, and on microscopy in 2 cases.

3 of the patients had either previous or concur tuberculosis; 2 had a long history of pulmonary dis

compatible with a diagnosis of bronchitis or bronchiectasis; and 1 had extensive pulmonary Hodgkin's disease.

Treatment with drugs was, on the whole, unsatisfactory, while symptomatic treatment with rest was most beneficial. Case histories are given for each patient.

C. J. La Touche

André, M., Orio, J., Depoux, R. & Drouhet, E. Histoplasmose africaine à grandes formes à localisations osseuses multiples. Évolution favorable après intervention chirurgicale et amphotéricine B. [**Large Cell Type of African Histoplasmosis with Multiple Skeletal Foci. Remission after Surgery and Amphotericin B**] *Bull. Soc. Path. Exot.* 1959, May–June, v. 52, No. 3, 345–52, 12 figs. on 4 pls. [12 refs.]

This is a case of African histoplasmosis in which bony structures became involved. Nevertheless, the patient (a male African aged 25 years from the Tchad area of French Equatorial Africa) responded favourably to surgical operation and the administration of drugs, especially amphotericin B.

In September 1957 he became aware of a lump the size of a plum situated over the right fronto-parietal region. It was painless and appeared to correspond with an underlying erosion of the right parietal bone. X-rays revealed rarefaction of the bony substance at the site, comprising a circumscribed area about 2 cm. in diameter with ill-defined borders, and appearing to involve the whole thickness of the skull.

At operation a very haemorrhagic mass of soft tissue was revealed which had insinuated itself through the cavity which was present in the bone. Moreover, it had spread horizontally between the skull and the meninges. It was an inflammatory lesion caused by a fungus which was proliferating in its yeast phase; it was a granuloma which included giant cells in which yeast forms were present.

After this operation the patient disappeared; only to return in February 1958. The operation site was found to have ulcerated and the floor of the ulcer was made up of very friable fleshy nodules of a violaceous colour which on pressure exuded a purple fluid. X-rays revealed a considerable extension of the rarefaction of the bone. No periosteal reaction was observed in its immediate vicinity, and in fact, the borders of the lesion were described as having the "wet sugar" appearance of "bad alloy".

Furthermore, a second lesion had presented at the level of the tubercle of the left tibia, and had developed with extreme rapidity since only a week had elapsed between its first appearance as a tumour and its appearance at examination as an extensive (4 cm.) ulcer. X-rays, as before, revealed extensive rarefaction of the bone and also, as previously, no periosteal reaction.

Curettage exposed an underlying cavity in the bone, filled with haemorrhagic soft tissue. Histological examination of the biopsy material from this tibial lesion revealed the same features as were observed previously in material obtained from the fronto-parietal lesion.

Cultures of biopsy material were positive and exhibited in due course the large, prickly (tuberculate) conidia which characterize the cultures of *Histoplasma capsulatum*. Animal inoculations resulted in widespread visceral lesions in which the large cells of the yeast phase of the variety *duboisii* were observed.

In addition to pre-operative prophylaxis with streptomycin and penicillin, chloramphenicol was administered as a cover against secondary infection as well as nystatin (4 million units daily) and sulphamerazine (50 mgm. daily). However, despite this treatment serious deterioration set in.

On the 1st March a symmetrically situated third lesion presented on the right tibia. Again an operation was performed which revealed much the same morbid features as were observed in the other lesions. After this operation, the patient, contrary to expectations, slowly rallied, and gained in weight. Moreover, the lesions showed signs of resolution.

On the 27th March therapy with amphotericin B was instituted, the patient receiving *per os* 2 gm. daily from the 27th March to the 7th April and then 3·75 gm. daily from the 7th April to the 21st April. However, owing to the onset of dizziness and nausea and general deterioration all drugs were withdrawn. Again, despite this set-back the patient rallied and his general condition progressed slowly while the lesions gradually resolved.

During the first week in June therapy with amphotericin B was resumed, and in July histological examinations of biopsies confirmed the clinical picture of recovery.

On the 24th September 1958, in order to confirm the resolution of the lesion in the right tibia a further biopsy was made and this was found to be sterile both by culture and by animal inoculation.

C. J. La Touche

González-Ochoa, A. Dos casos de esporotricosis curados con Griseofulvin. [**Two Cases of Sporotrichosis Cured by Griseofulvin**] *Rev. Inst Salubridad y Enfermedades Trop.* Mexico. 1959, June, v. 19, No. 2, 245–9, 6 figs.

The English summary appended to the paper is as follows:—

"A small epidemic of sporotrichosis, of two months duration was observed in three subjects: a father, 32, a mother, 24, and their son, 8 months old. The father and the mother had a lymphangitic type infection with ascending gummatous clinical form and the child presented a fixed type with verrucous clinical form. The father was treated with potassium iodide, the mother and son with griseofulvin. The mother received 1 gm. and the son 250 mg. daily divided in four intakes. The benefical results with griseofulvin were identical to those obtained with potassium iodide given to the father as control. Complete cure was obtained in the same length of time with both medications, three months of treatment for each patient. The cases continued under observation for four months after treatment was suspended and no relapse was observed. The antibiotic produced no collateral effects."

EDWARDS, Mercedes R., HAZEN, Elizabeth L. & EDWARDS, G. A. **The Micromorphology of the Tuberculate Spores of** *Histoplasma capsulatum*. *Canadian J. Microbiol.* Ottawa. 1960, Feb., v. 6, No. 1, 65–70, 10 figs. on 5 pls. [22 refs.]

SONNENSCHEIN, H., CLARK, H. L. & TASCHDJIAN, Claire L. **Congenital Cutaneous Candidiasis in a Premature Infant.** *J. Dis. Children.* Chicago. 1960, Jan., v. 99, No. 1, 81–5, 1 coloured fig. on pl. [13 refs.]

In this paper the authors describes a case of antenatal candidiasis in a premature infant. At birth this infant presented with a "diffuse papular and vesicular rash with large areas of exfoliation on the back, neck, postauricular region, the axillae, abdomen, groins and feet, especially marked around the ankles." Smears and cultures taken shortly after birth from the oral cavity and skin were positive for *Candida albicans*.

Nystatin therapy was instituted on the 4th day of birth consisting in the administration of "100,000 units in aqueous suspension by mouth q.i.d.; local swabbing of the oral mucosa with a suspension of the same strength; and nystatin-fludrocortisone ointment with neomycin and gramicidin (Myconef) to the skin twice daily". Improvement set in on the 6th day, and by the 8th day "the skin was almost clear". Clinical improvement continued until on the 11th day, "Topical medication was discontinued, except for the postauricular area". The baby was discharged "31 days after birth, in excellent physical condition".

From the nature of the cutaneous lesions at birth and from the fact that *C. albicans* could not be recovered from the vagina of the mother after delivery, the authors conclude that the infection had taken place *in utero*. Only a few cases of this nature have been recorded in the literature. *C. J. La Touche*

OSSWALD, H. & SEELIGER, H. P. R. Tierexperimentelle Untersuchungen mit antimykotischen Mitteln. 2. Mitteilung. Vergleichende Untersuchungen zur Wirksamkeit der peroralen und subkutanen Applikation von Amphotericin B am Versuchsmodell der mit *Candida albicans, Cryptococcus neoformans, Mucor pusillus* oder *Aspergillus fumigatus* infizierten Maus. [**Investigations with Antimycot Substances in Experiments on Animals. 2n Communication: Comparative Studies on th Activity of orally or subcutaneously administere Amphotericin B in Mice infected with** *Candic albicans, Cryptococcus neoformans, Mucor pusill* **or** *Aspergillus fumigatus*] *Ztschr. f. Immunitäts u. Exper. Therap.* 1960, Feb., v. 119, No. 2, 16 74. [16 refs.]

The English summary appended to the paper is follows:—

"Amphotericin B was administered orally as well subcutaneously to mice infected with *Candida albicar Cryptococcus, neoformans, Mucor pusillus* and *Aspe gillus fumigatus*. The oral route proved to be mo effective. In some experiments the death rates animals treated orally were markedly lower than animals treated subcutaneously."

TASCHDJIAN, Claire L., REISS, F. & KOZINN, P. J. **E perimental Vaginal Candidiasis in Mice; i Implications for Superficial Candidiasis Humans.** *J. Investigative Dermat.* 1960, Fe v. 34, No. 2, 89–94, 4 figs. [21 refs.]

KWAPINSKI, J. & MERKEL, M. Die Entwicklung v *Candida*-Kolonien unter dem Einfluss chemisch Fraktionen anderer Mikroorganismen. [**The Infl ence of Substances from Different Microorganism on the Growth of** *Candida* **Colonies**] *Zent. f. Ba* I. Abt. Orig. 1960, v. 177, No. 3, 410–20, 2 fi [14 refs.]

STEIN, J. M. & BURDON, Phyllis J. *Cryptococcus ne formans* **Infection of the Central Nervous Syste a Case treated by Amphotericin B, with Po mortem Examination.** *Ann. Intern. Med.* 196 Feb., v. 52, No. 2, 445–53, 5 figs. [12 refs.]

GADEBUSCH, H. H. **Infra-Red Spectra of Capsul Polysaccharides from Thirteen Strains of** *Cryp coccus neoformans*. [Correspondence.] *Natu* 1960, Feb. 27, v. 185, 610–12, 2 figs.

Communicable Diseases

The order in this section is:—**Tuberculosis; Venereal Diseases; General Infective Diseases; Other Communicable Diseases.**

For the bacteriology of these diseases see the section on Bacteriology below. For diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN.

TUBERCULOSIS

MERRETT, J. D. **Social Class Distribution of Respiratory Tuberculosis Notifications in Northern Ireland, 1949–53.** *Brit. J. Preventive & Social Med.* 1959, Oct., v. 13, No. 4, 215–21, 2 figs. [11 refs.]

During 1949–53 there were 3,777 out of 4,702 m notifications of respiratory tuberculosis whose a social class, stage of disease when notified was kno and who were aged 15 and over. There was an as ciation between stage of disease on notification a

social class. In social class I 37·7% of the cases were in stage 1 and 16·4% in stage 3 and in social class V 24·2% were stage 1 and 23·9% stage 3. The notifications showed a bimodal distribution with age, the first peak was at ages 15–24 and the second at ages 45–64 years. With a decline in the social class the second peak became more pronounced and in social class V exceeded the first peak. There is evidence of a bimodal distribution with age in the 3 stages of the disease on notification for each social class, but it is less clearly defined than in all groups combined because of fluctuations due to small numbers in some age-groups. In each social class as age increased the proportion notified in the more advanced stage of disease increased. This finding is influenced by the mass radiography programme which concentrates on the young adult population. About 15% of the population are examined by X-ray annually but many of these are in organized groups examined annually. In 1951 11·2% of the population aged 15–24 years were examined by X-ray but only 3·9% at ages 45–59 and 0·9% at ages 60 and over. *W. J. Martin*

STADLER, J. Epidémiologie actuelle de la tuberculose dans le canton de Vaud. [**The Epidemiology of Tuberculosis in the canton of Vaud, Switzerland**] *Ztschr. f. Präventivmed.* Zürich. 1960, Jan.–Feb., v. 5, Nos. 1/2, 17–36, 7 figs.

In the absence of compulsory notification the incidence of tuberculosis in Switzerland must be estimated from reports of deaths, tuberculin surveys and mass radiography surveys.

In the canton of Vaud [population 378,000] the tuberculin reactor rate at school entry (7 years of age) is 12–20% and at 15–16 years it is 22–48%. In the city of Lausanne (population over 119,000) the rates in 3,521 children aged 7, 9, 13 and 15 years were found to be 12, 20, 38 and 48% respectively. These figures show that the number of children infected was quadrupled in 8 years.

BCG vaccination is widely practised in Lausanne and by the age of 15 only 6% of children remain unvaccinated. The natural reactor rate is 48%, the post-vaccinal reactor rate is 46%, and 6% are non-reactors.

Tuberculin surveys in army recruits gave a reactor rate of 50·8% in 1,765 tested. There were differences according to the place of origin of the recruits. Those from rural areas had a rate of 24%, and those from urban areas 60%. A survey in adults showed that the reactor rate was 85% at 45–50 years and 62% after 71.

In 1955 49,489 persons were X-rayed. The results are incomplete. 53 cases of active pulmonary tuberculosis were discovered (2·2/1,000) of which three-quarters were new. Examples are given of the varying incidence of disease and varying success of the survey in the villages.

A whole army regiment numbering 3,292 men aged 20–36 years was examined in 1954. Active pulmonary tuberculosis was found in 5·5/1,000. Another regiment numbering 2,384 was examined in 1957; the discovery rate was 0·8/1,000. The difference in incidence was not thought to be due to a decline in the endemicity of tuberculosis but to the fact that the regiment with the high incidence came from an area with a low reactor rate, and consequently fewer of the young soldiers in it had had primary tuberculosis.

An X-ray survey in 3 factories with 3,093 workers of whom 2,857 were X-rayed yielded 1 new case per 1,000.

In spite of all control measures tuberculosis is still a serious problem in Vaud. The author advises BCG vaccination and mass radiography be extended even more widely than they are at present. *H. G. Calwell*

PAOLANTONIO, U. Alcuni aspetti attuali dell'epidemiologia tubercolare in Abruzzo e Molise. [**Some Aspects of the Epidemiology of Tuberculosis in Abruzzo e Molise**] *Lotta c. la Tuberculosi.* 1959, Oct., v. 29, No. 10, 1392–410.

Abruzzo e Molise is one of the large regions of Italy; more than one third of the total area of 1·5 million hectares lies over 1,000 metres above sea level. The result is that the climate is harsh and communications are poor. The population at the 1951 census was 1·7 million and there are only 2 centres with more than 50,000 persons. Housing and general hygienic conditions are very bad and there is often desperate poverty; agriculture is the main industry.

Deaths from tuberculosis have declined from 2,509 in 1887 to 218 in 1957, but morbidity not to the same extent though the figures are only those furnished to the various tuberculosis societies, as at present the disease is not compulsorily notifiable in Italy. The causes of error, however, are stated to be the same from year to year and the depressed economic conditions tend to make patients seek, rather than decline, assistance. In 1957 the number of ascertained cases (all forms) was 1,764, a rate of 1·1 per thousand.

The author then gives details of his own particular province, Aquila, which is the most mountainous of the 5 provinces of the region and where poverty is greatest. Males in whom the incidence is stationary are more affected than females, in whom it is decreasing, while between 1952 and 1957 there was a marked decrease in the 5–10 age-group and a marked increase in the 20–30 group. Females aged 10–19 have a higher rate than males but men over 50 a considerably higher incidence than women of comparable age. Considerable importance is attached to the fall in the young age-group as this may be due to a diminished ambient bacillary content.

The diagnosis on ascertainment was: cavitating forms 25%, primary 20%, bilateral non-cavitating 15%, non-pulmonary 15%. 35% of all ascertained cases were fatal within 1 year. In 1957 chest X-rays of 873 persons from a population of 53,288 gave 91 active and 220 inactive cases of tuberculosis, indicating a rate of 5·8 per 1,000. The author states, however, that though the primary forms have remained practically stationary, the evolutive forms have lessened, the widely disseminated types now run a less active course and isolated lesions are more common. This milder course he attributes not to any change in the organism itself or in the host but to the use of antituberculous drugs. He concludes that in this region tuberculosis

is primarily a family affair, hence prophylaxis must be directed towards better case finding, improvement of economic and housing conditions, BCG vaccination of Mantoux negative children, special surveillance of the chronic sputum positive patient, and of older persons, and free treatment. *W. K. Dunscombe*

VILARDO, S. & ZOTTOLA, V. Aspetti clinico-sociale della tubercolosi familiare in Provincia di Cosenza. [**The Clinical and Social Aspects of Family Tuberculosis in the Province of Cosenza**] *Riv. Italiana d'Igiene.* 1959, Sept.–Oct., v. 19, Nos. 9/10, 507–16. [42 refs.]

The authors have studied the records of 3,000 patients admitted to the tuberculosis hospital Mariano Santo of Cosenza in Calabria, and found that 1,000 of these came from households within the province. In 205 (over 20%) of these they found that 1 or more family contacts had also been affected. 18 were conjugal infections, 13 wives having contracted the infection from their husbands and 5 husbands from their wives. 58 child contacts had contracted the disease from one of the parents, the lesions found being primary in 17 of these children. 74 other contacts had contracted the disease from a brother [sisters are not mentioned]. In 28 households more than 1 family contact had contracted the infection, but some of these had been admitted to other hospitals and are not included in the above figures. It was not possible to examine every member of the 150 households which were investigated. [An indirect calculation from the figures given in this report suggests that some 193 family contacts were in fact found to be positive.] 2 children in each of 10 households, 3 in 4 and 4 or more in 2 had contracted the disease from one of the parents. In the case of "brotherly" contagion there were 2 cases in each of 59 households, 3 in 12, 4 in 2 and 5 in 1.

Duration of contact exposure to the source of infection ranged from 1 to 6 years. In 17 households a primary lesion—tuberculous meningitis in 6—was found after exposure to the parent's infection. In fact, the disease of the parent only came to light after some of these primary lesions in children.

Besides discussing diagnostic, prophylactic and other control aspects of the problem, the authors refer to the findings of a recent Parliamentary Inquiry into poverty in Italy: out of 11½ million families, 2½ (23%) were in poor circumstances—badly housed, undernourished and miserably clad. In Calabria 37% of families are living in poverty. *J. Cauchi*

SZABÓ, I. & KERTAY, N. Neue Angaben über die Verbreitung der extrapulmonalen menschlichen Tuberkulose vom Bovin-Typus in Ungarn. [**A Recent Examination of the Extent of Bovine Infection in Human Extrapulmonary Tuberculosis in Hungary**] *Acta Microbiologica.* Budapest. 1959, v. 6, No. 2, 157–9. [15 refs.]

The authors investigated 248 strains of *Myco. tuberculosis* isolated from patients with extrapulmonary tuberculosis. 147 had been recovered from urine, from pus, 12 from female genital organs and 64 fr other sources.

155 strains (62·5%) were found to be of human ty and 88 (35·4%) bovine. 5 cultures (2·1%) contain both types.

The percentage of bovine strains was 30 from uri 40 from pus, 50 from female genital organs and from other sources. The high incidence of bovi infection (although the number of cases is too sm on which to base a firm conclusion) demonstrates danger of infected milk and milk products to gi and women. The campaign for the eradication tuberculosis from cattle will improve this situation *H. G. Calwel*

WORLD HEALTH ORGANIZATION/UNICEF: Assis Tuberculosis Project. **Tuberculosis Survey Nairobi 1958–1959.** 38 mimeographed pp. numerous pp. of tables, 1 map & 7 figs. (1 foldi 1959, June.

Nairobi, with a population of 222,000, is the bigg city in East Africa, and its growth has been v rapid. Half the population is African, there are 85, Asians and 22,000 Europeans. About 300 cases tuberculosis are notified each year from the Afri population, and the number of deaths from tub culosis reaches ¼–½ of the number of notificati Tuberculosis is normally one of the 3 most frequen notified diseases, the others being malaria a dysentery. The African population contains an exc of males.

In 1958 a 10% random sample was taken of African population, and a tuberculin and pho fluorographic survey was made, sputum being exami by smear and culture where indicated. Not all persons assigned to the sample appeared for exami tion, but 9,962 did attend for the first appointm representing 92% of the sample. All ages over years were represented, the most numerous group be at age 20–29.

The results showed that persons with both relev X-ray shadows and positive sputum numbered 1·4 1,000 of the African population, and that in addi 7·6 per 1,000 had X-ray shadows which proba indicated closed tuberculous lesions. The total i dence was therefore about 9 per 1,000. Tuberc tests with 1 TU PPD were done by the intrader method and the incidence of positive reactions in m rose from about 5% at age 3 to 40% at age 15 to over 75% at age 35; the incidence in females not much different. Slightly over 4% showed vesic reactions. It was observed that the incidence positive reactions, and of vesicular reactions, higher in members of the Kikuyu tribe than in Kamba and Kavirondo tribes. In Kavirondo wo the proportion of slight reactions was relatively h and some of these may have been non-specific. general the Kikuyu tribe showed higher disease r than the others.

The report concludes with a comment that the served incidence of tuberculosis in this random sa

was much lower than had been expected, and that in a group of persons who came for examination on their own initiative, the incidence of open tuberculosis was 6 times as high as in the random sample.

Charles Wilcocks

KENT, P. W. **Tuberculosis—a Social Disease.** *East African Med. J.* 1959, Dec., v. 36, No. 12, 649–55.

This is a good paper. The author quotes OSLER, who described tuberculosis as a "social disease with medical aspects", and this is a point of view "particularly apposite to the Kenya of today". In Britain the decline in tuberculosis death rates was continuous and even during the period 1850–1948, and it was unaffected by the institution of dispensaries and the improvements in treatment; this was the period of continuous improvement in the general standard of living and the economic situation of the people. Since 1948 the decline in death rates has increased with the introduction of new drugs.

The author quotes authorities to indicate the poor state of nutrition and housing common in Kenya and neighbouring parts of Africa. The general situation is known, and policies have been laid down to deal with it; the difficulty has evidently been to devise means of raising the living standards of peoples who have never in their recorded history known or demanded better conditions. The author believes that the death roll from tuberculosis is over 10,000 per annum, and that there are 3 million infected persons. He quotes HEAF (writing about Africa), with approval: "Increase in protein diet, good housing and careful attention to the nurture of children will cause a greater decline in the incidence of the disease than modern treatment or vaccination". [And, of course, not only tuberculosis; like other socio-economic diseases the future of tuberculosis in now in the hands of statesmen and administrators rather than of doctors, in spite of BCG and the new drugs.]

Charles Wilcocks

BRIGGS, I. L. **A Mass Miniature Radiography and Tuberculin-Testing Survey in African Miners and their Dependents on the Copperbelt of N. Rhodesia, 1957–58.** *Central African J. of Med.* 1960, Jan., v. 6, No. 1, 6–13.

This mass miniature survey of surface copper mine employees and their dependents was carried out in 1957–58. All persons attending were tuberculin-tested and examined by X-ray with the exception of those under 4 years who were tuberculin-tested and only the reactors among them subjected to X-ray. The Heaf test with PPD was used. No person known to be ill was included in the survey.

Those whose miniature skiagrams showed an abnormality requiring investigation were recalled for clinical, bacteriological and further X-ray examination.

30,239 persons of all ages were tuberculin-tested and examined by X-ray of whom 17,659 (58·1%) were already participating in a trial of vole bacillus vaccination and their previous tuberculin state was therefore known.

130 cases of active tuberculosis were found (4·29/1,000 examined). The incidence in those known to have been reactors at least 28 months previously and in those known to have been non-reactors and unvaccinated was similar. The highest incidence (5·34/1,000) was found in persons seen for the first time. The incidence in those negative reactors who were vaccinated at least 28 months previously was 1·26/1,000.

Adult males had an incidence of active disease of 5·61/1,000 and adult females 2·8. The circumstances are described which lead to women being subject to a lower risk of infection than men.

Children were at risk from adults and not from one another. Primary disease accounted for 78·5% of the cases of active tuberculosis in them. The prevalence rate was 4·7/1,000.

The value of vaccination was demonstrated both in children and adult males. The results for women do not follow the same trend.

The author recommends mass miniature radiography of adult males combined with tuberculin-testing and vaccination. Families should be tuberculin-tested and vaccinated. Reactors must be examined by X-ray.

H. G. Calwell

GOERTTLER, V. Anerkennung der Tuberkulose eines Fleischers als Berufskrankheit. Obergutachten. [**Recognition of Tuberculosis in a Butcher as an Industrial Disease**] *Ztschr. f. ärztl. Fortbildung.* 1960, Feb. 1, v. 54, No. 3, 139–44.

A master butcher who had worked at his trade from 1930–54 and from 1945 onwards had been engaged particularly in the handling of internal organs, was taken ill with pulmonary tuberculosis in May 1954. The question then arose as to whether his condition could be regarded as being caused by his occupation. There was a conflict of opinion on this question between the medical experts representing the authorities for social and industrial hygiene and those representing industrial insurance. The problem was complicated by the fact that at first there was no adequate bacteriological evidence of tuberculosis and it was not till 1958 that it was reported that by special methods of investigation a sample of sputum obtained in 1956 was proved to contain tubercle bacilli of both human and bovine type.

Ultimately the author of this paper was requested by the Social Insurance Administration to answer certain questions and to give his opinion on the case. There is a full description and discussion of his reasoned opinion which was that the butcher had definitely been exposed to the risk of bovine tuberculous infection in the course of his work and hence was legally entitled to industrial compensation for pulmonary tuberculosis.

M. E. Delafield

KEPILÄ, A. Über Blutsenkung bei intrakutanen Alttuberkulinproben bei Lungentuberkulose. [**The Influence of Mantoux Testing on the Erythrocyte Sedimentation Rate in Patients with Pulmonary Tuberculosis**] *Ann. Med. Intern. Fenniae.* Helsinki. 1959, v. 48, Suppl. 30, 39 pp., 4 figs. [15 refs.]

The influence of the subcutaneous injection of Old Tuberculin has often been referred to in the literature on tuberculosis. Little attention has, however, been paid to the effect of the intracutaneous injection of tuberculin.

In this study the author sought the answers to the following questions:

(1) What is the effect of the intracutaneous injection of Old Tuberculin in doses of 0·1, 0·01 and 0·001 mgm. on the erythrocyte sedimentation rate (ESR) of patients with pulmonary tuberculosis?

(2) Is there any connexion between the rise in the ESR and the degree of local skin reaction?

465 patients with pulmonary tuberculosis (159 children, 168 women and 138 men) were the subjects of the investigation. The tuberculous lesions were considered to be stable in all cases, and care was taken to exclude any patient with an intercurrent condition that could have influenced the ESR.

The rate at 1 hour was found to be increased in 125 patients (26·9%) and to be decreased in 8 (1·7%). The degree of increase was proportional to the original rate, being greater when the original rate was higher. Increased rates were seen more frequently in females than in males.

There was a relationship between the amount of increase in the rate at 1 hour and the area of erythema of the skin at the site of the tuberculin test. Diameters of 19–20, 20–29 and 30–110 mm. accompanied rises in the ESR of 12, 23·1 and 40·5% respectively. With local erythematous reactions of 20–29 and 40–110 mm. in diameter there was a higher proportion of raised sedimentation rates in females than in males.

There was also a relationship between the degree of local induration of the skin and the raised sedimentation rate. Reactions of 19–20, 20–29 and 30–39 mm. were accompanied by increased sedimentation rates in 16·8%, 37·0% and 55·5% (10 out of 18). With local induration of 10–19 and 20–29 mm. the increase in the ESR was on average greater in females than males. *H. G. Calwell*

WICKS, C. A. **A Study of Five Hundred Consecutive Admissions to a Tuberculosis Hospital.** *Amer. Rev. Respiratory Dis.* 1960, Feb., v. 81, No. 2, 161–72.

This paper consists of observations on 500 consecutive admissions to the Toronto Hospital for Tuberculosis at Weston, Ontario, from January 1st to August 12, 1957. The number actually considered was 497, as 3 patients had more than one entry. The information was based on what was available from the files. The author very wisely defines clearly what he means by certain terms, and this avoids much co fusion. The 497 patients were grouped into 350 fi admissions, 84 re-admissions, 39 entering as transf from another hospital, and 24 for review of the dise status. 405 (81%) of the patients had tuberculosis the respiratory system as the most important proble 66 had other forms of tuberculosis predominate while 26 had only non-tuberculous disease. Of 350 patients who were available for this analy 40·9% were diagnosed because of symptoms, a 59·1% by routine examination of one kind or anoth As might be expected, 39% whose disease was detec because of symptoms had advanced disease, wher only 13% had advanced disease among those who w diagnosed by routine examination. Tubercle bac with definite resistance to streptomycin were isola on entry from 13 (4·6%) of all persons on first mission. Of these 13, all but 1 claimed to have H no previous treatment with streptomycin. Only patient on entry had definite resistance to PAS. patients (1·8%) of all first admissions had bac resistant to isoniazid; 4 of these 5 claimed to have H no previous treatment with isoniazid. Thus, 6·1% all patients on first admission had tubercle bac definitely resistant to one or more of the 3 dr studied.

As regards results, 276 patients were available assessment at 18 months after entry. Of these, were considered to have made satisfactory progr before or at regular discharge. None of these patie were known to have had relapse at the latest av able examination. A table is given showing the ef of drug resistance on therapeutic progress in hospital. Where there was definite drug resistance one or more drugs on entry without a history previous chemotherapy, the results in a small num of cases were nearly as good as the cases in wh there was no resistance; whereas when there definite drug resistance and a history of previ chemotherapy the results were very poor; only 36 being satisfactory. Of the 28 patients who had monary resection as part of their treatment 27 (96·4 showed satisfactory progress. Of the 39 patients w made unsatisfactory progress, 28 had far advan pulmonary tuberculosis, 25 had definite cavitati and all had positive sputum. On entry 50% of th patients had bacilli which had some degree of re tance to one or more of the drugs. A number tables are appended which bring out the points m in the text very clearly. *F. H. Youn*

TODD, R. McL. **Congenital Tuberculosis: Report a Case with Unusual Features.** *Tubercle.* 19 Feb., v. 41, No. 1, 71–4.

MARTIN, C. J. & MILLER, W. T. **Pneumonectomy the Treatment of Pulmonary Tuberculosis. After History.** *Amer. Rev. Respiratory* 1960, Feb., v. 81, No. 2, 184–8, 1 fig. [11 refs

This is a review of the results of pneumonect carried out on 204 patients during a 9½ year pe

from January 1946 to June 1955. It includes 16 on whom the pneumonectomy was performed during the 'adequate chemotherapy era". As the anniversary method which is applied to this study generally revealed no significant deviation from the others for the first 2 years these 16 are included.

The patients are divided into 3 groups: those who had previous thoracoplasties, those who had concomitant thoracoplasties, and those who had not had thoracoplasties. Of the 204 cases of tuberculosis, 60% of the patients had inactive tuberculosis 1 year after surgery; by the second anniversary this was increased to 70%, and at the third anniversary less than 2% had active disease. On the eighth anniversary of their surgery 21% were dead. 134 of the patients in this study (66%) had pneumonectomies with thoracoplasties following the resection within the 2 weeks that this was planned to be carried out. When this group was compared with the total group there was no significant difference at any anniversary in the number expected to have active or inactive disease or to have died of tuberculosis.

Of the 54 (26%) of the pneumonectomies completed after the failure of thoracoplasty to control the disease, the proportion having inactive tuberculosis or dying was about the same as in the total group. 16 of the patients had no thoracoplasty, either before or after pneumonectomy. The number of patients, and period of observation, were insufficient to act as a basis from which conclusions could be drawn, but no significant deviation from the general results was noted.

88% of the patients dealt with by pneumonectomy had far advanced pulmonary tuberculosis on admission to the sanatorium, and all had some disease in the unoperated lung. Full details are given in an elaborate table.

F. H. Young

MIDDLEBROOK, G., COHN, M. L., DYE, W. E., RUSSELL, W. F. & LEVY, D. **Microbiologic Procedures of Value in Tuberculosis.** *Acta Tuberculosea Scandinavica.* 1960, v. 38, No. 1, 66–81. [36 refs.]

The authors state that in spite of the use of combined drug therapy in tuberculosis the sputum of 10–20% of previously untreated patients in the United States failed to become bacteriologically negative without ancillary collapse procedures or surgical intervention. Most of these failures were accompanied by a relatively early emergence of a bacterial population resistant to only 1 of the antimicrobial drugs administered.

Experimentally they found that when an adequate concentration (0·2 μgm./ml. or more) of isoniazid was present in the test medium, those colonies which were recovered on the plates contained only isoniazid-resistant mutants. Only streptomycin-resistant mutants were present in the colonies which grew on plates containing adequate concentrations (2·0 μgm./ml. or more) of streptomycin. The combination of the same adequate concentrations of both drugs completely prevented the appearance of any colonies. On the other hand when a concentration of streptomycin (1·0 μgm./ml.) inadequate to inhibit the growth of all susceptible organisms was present, both streptomycin-susceptible and streptomycin-resistant tubercle bacilli were recovered. When this inadequate concentration of streptomycin was combined with an adequate concentration of isoniazid, those few colonies which were recovered were shown to be isoniazid-resistant and streptomycin-susceptible.

The mechanisms of action of both drugs are probably unrelated and independent. When both drugs were present in the test medium in concentrations adequate to sterilize all multiplying parent drug-susceptible bacterial cells, they prevented the growth of single-drug-resistant mutants by cross-sterilization.

The authors conclude that the clinical implications of these experiments are: (1) In order to sterilize those tubercle bacilli which are multiplying at least 2 drugs to which they are susceptible should be administered in quantities sufficient to produce bactericidal concentrations. (2) Failure to achieve the minimum inhibitory concentration of both drugs at the sites of multiplication should result in persistent excretion of drug-susceptible bacteria. (3) Failure to deliver an adequate concentration of 1 of the 2 drugs will result in the selection of mutants resistant to the action of the second drug, the one delivered in adequate concentration. Hence for the best chemotherapeutic results it is necessary that the population of tubercle bacilli be characterized as to its susceptibility to the antibacterial drugs which may be used. They consider that clinically significant drug susceptibility is present when less than 1% of the organisms yielding colonies on the control plates are able to grow and produce colonies on plates containing streptomycin, 2·0 μgm./ml., or isoniazid, 0·2 μgm./ml., or PAS, 2·0–5·0 μgm./ml.

The routine bacteriological procedures employed at the National Jewish Hospital at Denver, Colorado, is given in detail.

It has been known for some time that isoniazid is altered metabolically in the human body to chemical derivatives which have little or no antimicrobial activity, and this occurs at widely different rates in different individuals. Hence a rapid inactivator may need as much as 4 times the amount needed by a slow inactivator in order to attain a level consistent with adequate bactericidal effect. This does not occur with streptomycin; but it has been shown that there are consistent differences in the serum concentration of streptomycin achieved by different subjects on the same dosage. However, antimicrobial action is antagonized by substances present in tuberculous lesions, as well as by the number of bacilli exposed to its action; hence it would be rather hazardous to correlate the concentrations of streptomycin achieved in the serum with the actual amount of drug delivered in an active form to the foci where tubercle bacilli multiply.

The chemical methods thus far described for the determination of isoniazid serum levels have not proved practical for the antimicrobially active moiety, hence a microbiological assay was developed in the Denver institution and is found to be sufficiently accurate and technically simple for the purpose. The details for the microbiological assay for serum isoniazid are given

in full. Similarly it is recommended that the microbiological assay for streptomycin developed in the institution should be used.

The authors conclude that it is reasonable to postulate that increasing the dosage of each drug should largely eliminate such evidence of inadequate delivery of drugs as the emergence of organisms resistant to 1 of the 2 drugs. However, with higher doses there is significant incidence of drug reactions; hence the appropriate and adequate chemotherapy should be based on choosing the 2 appropriate drugs by drug-susceptibility testing of the patient's bacilli, and the dosage of each drug to be administered by establishing the amount that is sufficient to produce at least the minimal antibacterial serum level, as demonstrated by properly performed microbiological assays. When these principles were applied to 153 consecutively admitted patients to the National Jewish Hospital who excreted isoniazid- and streptomycin-susceptible bacilli, all but 1 converted to bacteriologic negativity within the first 6 months of chemotherapy, and on follow-up examination performed 18–48 months after the start of chemotherapy only 2 relapses were revealed among the 144 patients available for study.

[It is sufficient to say that this paper does not fall below the standard which is expected from papers emanating from the National Jewish Hospital at Denver.] *F. H. Young*

United States Pub. Health Service. **Sequential Use of Paired Combinations of Isoniazid, Streptomycin, Para-Aminosalicylic Acid, and Pyrazinamide. Tuberculosis Therapy Trial.** *Amer. Rev. Respiratory Dis.* 1959, Nov., v. 80, No. 5, 627–40, 12 figs.

Observation on 6,000 patients suggests that tuberculous subjects still infectious after 6 months of continuous treatment are likely to remain so in the absence of supplementary procedures. With isoniazid-PAS during the early weeks the response to treatment is prompt and steady. At each successive period fewer patients continue to excrete tubercle bacilli. This continues at a fairly rapid rate to the first 16–20 weeks then more slowly until virtually no further change occurs after 24 weeks. This finding persists whether the disease is advanced or cavitated, but of course the final percentage of those converted is much less in the advanced or cavitated disease cases.

In 1953 a trial was undertaken to determine whether chemotherapy effectiveness could be prolonged by a change in the combination of drugs after the sixth month. Only isoniazid, streptomycin and PAS were available at that time. Substitution of streptomycin for isoniazid after 24 weeks had no apparent effect, but a switch to isoniazid from streptomycin produced further bacteriological change. The optimum effect of changing chemotherapy might be expected when the second course contained 2, instead of 1 previously unused antimicrobial agents. After a trial had shown that liver damage from the use of pyrazinamide was not a serious sequela, this drug was paired with the other 3, giving 5 regimes which were compared. 1,882 patients were randomly allocated to the 5 regimes table giving their chacteristics is appended; fortuna the number of defaulters was similar in each regi An appreciably higher percentage of the patients daily streptomycin and pyrazinamide were unable tolerate this combination when compared with other combinations. Regime 5 (daily streptom with pyrazinamide for 16 weeks, followed by isoni and PAS for a further 16 weeks) was the only cor nation which showed any advantage over isonia PAS for the whole 32 weeks. Radiologically regime had a slight though not statistically signifi superiority.

As regards the presence of tubercle bacilli, regim produced a more rapid reversal of infectiousness t any other. After 12 weeks of treatment only 25% the patients were still excreting tubercle bacilli. A a switch to isoniazid-PAS, reversal of infectious again occurred, and less than 5% were still infect after 32 weeks. This regime had an early advant and a slight, though not statistically signifi superiority at the end of the treatment. Details of loss of susceptibility to the drugs are given, but u none of the regimes were the bacilli resistant to 4 drugs and very few to 3 drugs. When the pati on regimes 1 and 4 were divided into far adva cavity cases and others, definite advantage was fo at the end of 32 weeks in regime in the far adva cavity cases, but not in the other group. At the of 32 weeks only 6·8% of the patients on regim compared with 14% on continuous isoniazid-PAS had a positive culture. It was concluded that regi is a promising regime for patients with far adva cavity disease, and it is precisely for those patients a generally less favourable prognosis that the th peutic benefit would outweigh the risk of intolerance. [This is a very valuable paper and m careful study.] *F. H. You*

Hobby, Gladys L. & Deuschle, K. W. **The Us Riboflavin as an Indicator of Isoniazid Inges in Self-Medicated Patients.** *Amer. Rev. Res tory Dis.* 1959, Sept., v. 80, No. 3, 415–23, 5 fi

Now that ambulatory treatment by drugs in handling of pulmonary tuberculosis has become common, the problem of detection as to whether patients are taking the drugs has become of increa importance. This is especially so in the back countries where ignorance and the difficulties language may lead to the drugs not being ta Many therapeutic agents are complex chemical pounds, the detection of which is often diff because the laboratory proceedings require more paratus and skill than is usually available in the This report gives a new approach to the solutio the problem, though it reports the detection isoniazid rather than PAS.

The idea is that a tracer indicator should be a to the drug in question, and that this tracer shoul estimated in the urine, rather than the drug i The authors use riboflavin incorporated in the ta or capsules of isoniazid. These were supplied by manufacturer in the form of tablets containing 50 m

f isoniazid, with 2, 5, and 8 mgm. of crystalline iboflavin added. A very full and detailed account of ne laboratory procedures necessary to detect and esti- nate the riboflavin is given. Experiments were done n a number of normal patients which showed that they were not taking additional vitamins in their iet the normal concentration of riboflavin was seldom n the excess of 1·5 μgm. and hardly ever more than ·4 μgm. per ml. of urine. When the tablets were eing taken more than 2·4 μgm. per ml. of urine as found for 24 hours.

The attributes necessary for a satisfactory tracer are hen described. It must not interfere with the action f the therapeutic agent in question; it must meet all he requirements of a safe and effective drug, that is o say it must be readily absorbed when administered y the same route as is used by the therapeutic drug n question, and must be excreted in the urine over period of 12–24 hours; it must be non-toxic, non- llergic, easily detected in a low concentration, and hould cause no unpleasant colour or odour in body luids. The tracer material must be cheap, palatable nd stable. Riboflavin seems to meet essentially all hese requirements; its main drawbacks are; (1) It is resent in varying concentrations in many foods, and normally excreted in the urine in low and variable mounts, but in a normal diet this does not matter. 2) It is present in most vitamin preparations which the patients often take without the physician's knowledge. n some cases these disadvantages may give rise to the dea that the drug is being taken when really it is not, ut especially if vitamin preparations can be excluded he test is very satisfactory and will detect most defaulters.

F. H. Young

Debré, R., Noufflard, H., Brissaud, H. E. & Gerbeaux, J. **Infection of Children by Strains of Tubercle Bacilli initially resistant to Streptomycin or to Isoniazid.** *Amer. Rev. Respiratory Dis.* 1959, Sept., v. 80, No. 3, 326–39, 1 fig. [17 refs.]

The development of strains of tubercle bacilli esistant to the available anti-tuberculous agents is a serious public health problem. The risk represented y such organisms has therefore been reassessed by he present authors by studying the strains of tubercle acilli with which children have been infected.

Strains of tubercle bacilli isolated from patients dmitted with primary tuberculosis to the Hôpital des nfants Malades, Paris, and the Hôpital Léon Bernard, Brévannes, between 1948 and 1958 were examined for heir sensitivity to streptomycin and isoniazid. The study was limited to the strains isolated from patients ot previously treated or treated for less than one week with the corresponding anti-tuberculous drug.

From 1950 to 1957, 18 of 394 strains of tubercle acilli were found to be resistant to streptomycin and 4 (or possibly 5) of 168 strains were resistant to soniazid.

Resistance to streptomycin in untreated patients with meningitis was first observed in 1949 and was con- sidered to have become a serious problem by 1952. Since the introduction of isoniazid the increase in primary resistance to streptomycin has ceased.

From detailed epidemiological considerations the authors conclude that there is a time-lag between the introduction of an anti-tuberculous drug and the appearance of primary tuberculosis due to tubercle bacilli resistant to that drug. The importance of multiple-drug therapy in tuberculosis and the isolation of sputum-positive patients is stressed.

Max Sussman

Larkin, J. C., Jr. **Results of Therapy with Thiocarbanidin used with Isoniazid or Streptomycin.** *Amer. Rev. Respiratory Dis.* 1960, Feb., v. 81, No. 2, 235–40, 1 fig.

This paper tries to assess the value of thiocarbanidin, a thiocarbanilide derivative, as a substitute for PAS when the latter is used as a companion drug with streptomycin or isoniazid. The paper starts with a short review of the literature available about this drug and its antituberculous activity *in vivo* and *in vitro*. The study was made, commencing in July 1958, both on previously untreated and re-treated cases. The analysis of the final results extends to April 1 1959, for those patients still in the study. 23 patients received isoniazid, 300 mgm. daily, and 1 gm. of thiocarbanidin daily in a single dose. 24 patients received the same dose of isoniazid, together with 12 gm. of PAS daily. 7 patients received streptomycin and thiocarbanidin in the same dose, and 7 streptomycin and PAS, 12 gm. daily. In the re-treatment group, the numbers were 18, 7, 15, and 6, respectively. In few of the patients did the course extend for more than 8 months.

After eliminating the patients whose sputum was only positive prior to admission to the hospital reversal of infectiousness occurred in 8 patients (35%) who received isoniazid and thiocarbanidin, 12 patients (55%) who received isoniazid, and PAS, in 1 patient (17%) who received streptomycin and thiocarbanidin, and in 2 patients, (29%) who received streptomycin and PAS.

The results of the re-treatment of patients were, as might be expected, considerably worse, but the tendency was the same as in the first group.

At the conclusion of treatment, 9 out of 23 patients who still had bacilli in the sputum (39%), had organisms resistant to isoniazid in the first group, as against 1 patient out of 22 (5%) in the isoniazid-PAS group. Similarly, 4 out of 6 patients (67%) had resistant organisms in the streptomycin-thiocarbanidin group, as against 3 out of 7 patients (43%) in the streptomycin-PAS group. The resistance, of course, refers to the isoniazid or streptomycin respectively.

The only unfavourable radiological cases occurred in the patients who were being treated with thiocarbanidin. Very little evidence of toxaemia to this drug was found but the blood concentration showed that the absorption from the alimentary tract was poor.

It was concluded that from the limited data available thiocarbanidin is of doubtful value as used in this study.

F. H. Young

DALEY, D. & SMITH, W. G. **Hypersensitivity to PAS Simulating Glandular Fever (Infectious Mononucleosis).** *Tubercle.* 1960, Feb., v. 41, No. 1, 68–70. [12 refs.]

ORGANICK, A. B. **Kanamycin-Tetracycline in Chronic Pulmonary Tuberculosis with Comments on the Auditory Toxicity of Kanamycin.** *Amer. Rev. Respiratory Dis.* 1960, Feb., v. 81, No. 2, 256–8. 1 fig. [Refs. in footnotes.]

This report is concerned with the occurrence of auditory toxicity in 12 patients with chronic tuberculosis who received kanamycin 1 gm. per day intramuscularly, and tetracycline 2·0 gm. per day by mouth. It was hoped to continue this regime for 6 months; this, however, was not achieved, because toxicity, mainly auditory, occurred and caused the cessation of the trial. The auditory toxicity occurred rather abruptly, and caused the discontinuation of the kanamycin in 11 out of the 12 patients. Subjective complaints were the rather sudden onset of tinnitus, followed by complaints of hearing loss, after receiving 49 to 144 gm. of kanamycin. 6 patients had pre-treatment audiograms, and serial audiograms were made. All of these had had streptomycin in the past, and all the pre-treatment audiograms were abnormal showing pre-existing high-tone deafness. In these patients it was possible to document further perceptive loss in the high frequency range of 5% to 25%. In the 4 who had no pre-treatment audiograms it was believed that the kanamycin was responsible for further loss. 7 patients were followed up and in no case did high-tone perception improve 3 months after cessation of kanamycin. In 4 patients slight further loss occurred. Vestibular toxicity was less common than hearing loss, and developed in only 2 patients. Renal toxicity in the form of a rising blood urea nitrogen was the cause of discontinuation of kanamycin in only 1 patient. There was no true reversal of infectiousness although 3 patients showed some transient reductions in the acid-fast bacilli on microscopy. Slight X-ray improvement occurred in only 1 patient.

Curiously enough the tetracycline was poorly tolerated, and half of the patients were unable to take this drug for more than 6 weeks. *F. H. Young*

HUTÁS, I. & NYIREDY, G. **Comparative Functional Studies in Cases of Exudative Pleurisy treated with and without Corticoids.** *Acta Tuberculosea Scandinavica.* 1960, v. 38, No. 1, 12–17, 1 fig. [27 refs.]

The authors seem convinced that pleural effusions clear up more quickly if corticosteroids are used in addition to antibiotics. This paper sets out to examine the diminution of permanent lung pleural damage that can be obtained by the use of these drugs.

The authors in Budapest treated 20 patients with exudative pleurisy with corticosteroids and antibiotic agents, and 20 who received antibiotics and were aspirated. All patients had little or no parenchymal disease. On an average the patients received 1 month's corticosteroid treatment, the dose was 20 to 25 mgm. of cortisone per day, and 20 units of corticotro per week; more recently they used 10 to 25 m of prednisone per day. When the disease cleared patients were ordered to come for follow-up stu lasting from 3 months to 1 year. Only 6 patients to be aspirated more than twice, in contrast to patients in the control group. 4 of the patients g corticosteroids developed pleural adhesions, but a s ficant callus was found in 1 only. In 3, the c costeroid treatment was not started immediately, it became less efficient the longer the time that been allowed to elapse. In 1 acute case only d large callus appear, as against 8 cases in the co group. In 9 of the treated group the authors c not observe any tension or adhesion of the diaphr

The respiratory function results are consider better in the corticosteroid treated group, as show the following table.

Respiratory function results in corticosteroid treat patients and the control group.

	VC	MBC	Vems
Corticoid ...	3350 ml.	73·61 litres	80
Control ...	3077 ml.	56·19 litres	6

F. H. You

TANDON, R. N. & KHANNA, B. K. **Pulmonary Tu culosis following Corticosteroid Therapy Tuberculous Meningitis. (A Report of 2 Ca** *J. Indian Med. Ass.* 1959, Nov. 1, v. 33, N 369–71. [29 refs.]

This article reports 2 patients in whom pulmo tuberculosis developed after corticosteroid therapy antimicrobial drugs for tuberculous meningitis. I first pulmonary tuberculosis developed about 5 m after the corticosteroid therapy had ceased, and i thought that the patient had carried on with her tuberculous drugs as instructed, though this is proved. In the other patient the pulmonary tuberc developed when the patient was still under ade antituberculous drugs and corticosteroid therapy. patient had been in hospital the whole time, so the tinuance of antituberculous drugs is taken for gra However, the fact that she was on PAS and iso does not make this supposition entirely proved. development of pulmonary tuberculosis in patients tuberculous meningitis who are responding factorily to treatment with antituberculous drugs corticosteroids is certainly very rare. The p genesis of the relapse phenomenon is discussed.

F. H. Yo

SHAH, R. S. & BHAVSAR, C. M. **Tuberculous M gitis.** *J. Indian Med. Ass.* 1959, Nov. 1, No. 9, 364–8.

This study aims at conducting a preliminary s in order to find out at a later date the best pc treatment regime suited to the conditions in Ind

2 regimes were tried. Group I received injecti streptomycin plus isoniazid—43 cases. Group ceived injection of streptomycin and isoniazid,

eroids—27 cases. 7 patients were treated by other ethods. Of the 77 patients studied, 21 died and 56 urvived. Of the 21 who died, 18 died within the rst week of admission most of whom were in mori- und condition. This gives a survival rate of 72·7%. he survivors are graded as grade 1, survivors who re mentally and physically normal with normal or lightly changed cerebrospinal fluid findings; Grade 2, urvivors who showed few changes mentally and physi- ally but in whom the cerebrospinal fluid changes were narked; Grade 3, survivors who had not benefited by he treatment at all. Grade 3 should be considered o be a failure of treatment. If the number of patients vho died is added to the number who survived in Grade 3, failure occurred in about 42% of the group or which steroids were used in addition to the strepto- nycin and isoniazid, compared with 52% where they were not used. The authors think that steroids should be used in addition to the antituberculous drugs in the reatment of tuberculous meningitis in India.

F. H. Young

POLLOCK, T. M. **BCG Vaccination in Man.** *Tubercle.* 1959, Dec., v. 40, No. 6, 399–412, 2 figs. [Numerous refs.]

This informative review is based on an extensive perusal of the literature on the subject. Many of the items mentioned in the bibliography have been noticed in the *Bulletin.*

The contribution that BCG vaccination may be expected to make to the control of tuberculosis will vary with local circumstances. It would for example be greater in India, with some 2½ million tuberculous persons and as yet insufficient public health services, than in England.

An indication of the effect of mass vaccination of a single age-group in England (13 year-old children) is given in the report of the Medical Research Council's Tuberculosis Vaccination Trial [this *Bulletin*, 1956, v. 31, 621; 1960, v. 35, 253]. In the first 5 years after entry the incidence of tuberculosis in the vaccinated group was about one-sixth of that in the non-reactor vaccinated group.

The incidence of the disease in the group of original reactors indicates that many of the cases of tuberculosis notified in adolescents or young adults occur in reactors who have been ineligible on that account for vaccination. If the reactor rate in late childhood is high vaccination should be done in early childhood.

The application of mass vaccination must accord with the epidemiological situation at the time. "In contemporary England BCG can make a unique and important contribution to the reduction of tuberculosis in young adults."

H. G. Calwell

SUTHERLAND, I. **An Estimation of the Scope for BCG Vaccination in preventing Tuberculosis among those aged 15–19 Years in England and Wales at the Present Time.** *Tubercle.* 1959, Dec., v. 40, No. 6, 413–24, 3 figs. [11 refs.]

Since the beginning of the Medical Research Council's trial of vaccination against tuberculosis in 1950 the risk of exposure to tuberculous infection has decreased substantially in England and Wales. Sutherland has taken this change and the falling reactor rate which accompanies it into account in the present statistical assessment of the scope of BCG vaccination. The most recent year for which data are available is 1958. The statistical methods used are described.

The incidence of tuberculosis in 1958 among those young people aged 15–19 years who were reactors at 14 years of age is estimated at 0·426/1,000. The estimated incidence in a population similar to that in the Council's trial was converted to an estimate appropriate to the population of England and Wales, which was 0·365/1,000. This represents that part of the total notified incidence attributable to those already reactors at 14.

The incidence rate attributable to those who were non-reactors at the age of 14 was 0·601/1,000. It was estimated that 1,400 cases of tuberculosis in persons aged 15–19 years could have been prevented in 1958. This number was about 2,950 in 1953. If the trend of decline in risk of exposure to infection continues, vaccination of all non-reactors aged 14 years now (1959) would apparently reduce the incidence when they reach the age of 15–19 years by rather less than half, compared with the 1953 figure of 60% for notifications which could have been prevented by BCG.

H. G. Calwell

SPRINGETT, V. H. **BCG Vaccination and Tuberculosis in Birmingham. A Study of Notifications related to Vaccination of Children before leaving School.** *Tubercle.* 1959, Dec., v. 40, No. 6, 432–42, 4 figs.

Birmingham is an industrial city with a population of some 1,100,000. BCG vaccination was offered to schoolchildren aged 14 years from 1954 onwards. About 75–80% of parents consented to their children being vaccinated, and 85% of those presented were found to be non-reactors and were vaccinated.

Notifications of tuberculosis between the ages of 10 and 19 years were analysed for the period 1950–58. These included notifications for the groups that should have been fully covered by the scheme and those partially covered. For the 15-year-old group the fall in notifications after 1955 was significantly greater than would have been expected from the experience of those aged 10–13 and 18–19 years. It was of the order of 0·7/1,000 per year.

Another assessment was made by comparing calculated notification rates in non-reactors who were vaccinated and in reactors (who were not vaccinated) with the corresponding rates in those who did not participate in the vaccination scheme. There was a reduction of the order of 50% or 0·6/1,000 per year in favour of the participating group as a whole.

"Statistically the evidence . . . cannot be taken as establishing the value of BCG vaccination. Practically, and taken in conjunction with the Medical Research Council Trial [this *Bulletin*, 1956, v. 31, 621 and 1960, v. 35, 253] the evidence fully justifies the use of BCG in children about to leave school in Birmingham and similar communities." Financially the cost of

vaccination is less than the cost of dealing with the cases prevented. *H. G. Calwell*

GRIEP, W. A. Onopgeloste problemen bij de tuberculosebestrijding. [**Unsolved Problems in the Campaign against Tuberculosis**] *Nederl. Tijdschr. v. Geneesk.* 1959, Sept. 26, v. 103, No. 39, 1968–74, 12 figs.

Tuberculosis mortality curves for the Netherlands for the present century are presented, from which it can be seen that the mortality has been steadily decl ing over the whole period in the absence of any as ciation with new advances in treatment. At the sa time the maximum mortality has shifted to ol age-groups, and also the age at which the first inf tion occurs. Persons who experience their fi infection at the time of puberty have a greater pr ability of developing pulmonary tuberculosis than th infected in childhood and the success of public hea measures among children may therefore cause a pa doxical increase in morbidity in the older age-grou *D. J. Baue*

VENEREAL DISEASES

WILLCOX, R. R. **Reactions to Antibiotics. Their Importance in Venereology.** *Brit. J. Venereal Dis.* 1959, Dec., v. 35, No. 4, 208–19, 2 figs. [48 refs.]

This article deals with a number of antibiotics but is concerned chiefly with penicillin. Reactions may be divided into (a) toxic, systemic or local, (b) microbiogenic sequelae, lysis, overgrowth, resistance etc. and (c) allergic, skin or anaphylactic reactions. Streptomycin has a selective action on the 8th nerve and chloramphenicol on the haemopoietic system; of the "lysis" reactions therapeutic shock and therapeutic paradox are the most important; microbial overgrowth of resistant staphylococci and monilia constitute the greatest danger, the former proving a serious problem in hospitals; bacterial resistance is well shown by the increasing doses of penicillin needed to cure gonorrhoea.

Allergic reactions include skin reactions and anaphylactic reactions; the latter are often serious and not rarely fatal.

Precautions against penicillin reactions should include careful history taking, skin, ocular and other similar tests, availability of emergency treatment and avoidance of the indiscriminate use of antibiotics [incidentally, adrenaline should always be immediately available].

Antibiotics should be used only when there are well-tried therapeutic and prophylactic indications.

This is a most informative and authoritative article and should be studied not only by venereologists but by all who use these remedies. *T. E. Osmond*

MAGNUSON, H. J., THOMAS, E. W., OLANSKY, S., KAPLAN, B. I., DE MELLO, L. & CUTLER, J. C. **Inoculation Syphilis in Human Volunteers.** *Medicine.* Baltimore. 1956, Feb., v. 35, No. 1, 33–82, 2 figs. [56 refs.]

This is a good account of well planned experiments carefully carried out in 1953. The literature of the subject is first reviewed, then the experimental work is reported.

Those inoculated were volunteers, all males over age of 21, and were prisoners at Sing-Sing. TH mostly came from urban centres in the lower N York State. Their original syphilis was treated centres where records were available. 54 of volunteers had syphilis or untreated syphilis, and th were 8 non-syphilitic volunteers.

The experiments and their results are next record and discussed. It is pointed out that the method challenge was probably unusually severe upon the h resistance. The findings emphasized that patients w have had syphilis, even though cured in the prim stage, are immunologically never the same. A p vious syphilitic infection of sufficiently long durat may produce considerable resistance to subsequ challenge. "The patient who presumably has least immunity may develop a darkfield positive les but will differ immunologically in the accelerated p duction of circulating antibodies. In patients presu ably having somewhat greater immunity, the organis may be extremely scanty in the lesions which deve at the site of inoculation. In some lesions, it may impossible to demonstrate the organism. The pres data would suggest that such patients would show increase in the titer of serologic tests."

Gummata developed in 2 previously well trea patients which shows that the particular type of alle that leads to the production of gummata may per for years in spite of treatment. Such lesions may the response to re-infection.

It was found that most results of the present exp ments could be predicted from experimental findi in animals. However, the decline in immunity v time suggested by the present experiments and wh had not been foreseen may be due to the relati short life of experimental animals. It was also fo that acquired immunity apparently develops somew more slowly in man than in the rabbit. All volunteers were given adequate treatment at the la by the end of 4 months after inoculation with li *Treponema pallidum*.

The paper is a most important one and should read by all interested in the subject. The auth summary gives a useful brief survey of the work is as follows:

"The intracutaneous inoculation of 4 graded doses of virulent *T. pallidum* (Nichols' strain) into each of 8 non-syphilitic human volunteers gave a 50% infectious inoculum of approximately 57 organisms. The 50% infectious inoculum in rabbits given the same suspension was approximately 23 organisms. Thus, the Nichols' strain of *T. pallidum* has maintained a high degree of infectiousness for man." [It has been maintained in rabbits since 1912.]

"The intracutaneous and subcutaneous injection of 50,000,000 heat-killed *T. pallidum* produced an anamnestic rise in TPI antibodies in some patients previously treated for early syphilis but failed to produce significant increases in reagin titers. No changes in circulating antibodies were demonstrated in non-syphilitic control patients given this same antigen.

"Fifty-four volunteers who had had previous syphilis were inoculated intracutaneously at a single site with 100,000 virulent *T. pallidum*. All but 5 of these patients had had presumably adequate therapy for their earlier infection. Two of the treated patients had to be discarded from the study because they received penicillin before the results of challenge inoculation were known.

"The 5 patients with untreated latent syphilis showed no clinical or serologic response to challenge and are presumed to have been resistant to superinfection.

"Of 11 patients previously treated for proved or presumed early syphilis, 9 developed darkfield positive lesions, while 2 developed darkfield negative lesions. All responded with increased STS titers and were considered to have been infected by the virulent inoculation. Patients in this group developed reagin and TPI titer increases much more rapidly than did the non-syphilitic controls.

"Of 3 patients previously treated for proved or presumed reinfection, one developed a darkfield positive lesion, another a darkfield negative lesion, both associated with increased STS titers. One patient showed no clinical or significant serologic response to challenge.

"Of 26 patients previously treated for proved or presumed late latent syphilis, 10 were considered to have been infected. One developed a darkfield positive lesion, 9 darkfield negative lesions all with increased STS titers. One of the latter lesions was a gumma. Three patients developed darkfield negative lesions not associated with STS titer increases, while 13 patients showed neither clinical nor serologic change.

"Among 5 patients treated for proved or presumed congenital syphilis, darkfield positive lesions developed in 1, 3 developed a darkfield negative lesion associated with increase in serologic titer, one of which lesions was a gumma. One patient showed no clinical or serologic evidence of infection.

"Of two patients previously treated for asymptomatic CNS syphilis, one may have developed a CNS reinfection, the other showed no evidence of reinfection.

"Patients who had previously had syphilis differed from non-syphilitic controls in their reaction to infection. In a general way, this reaction was influenced by the duration of their original infection prior to treatment, but there was considerable difference among individuals.

"There is some evidence to suggest that the administration of heat-killed *T. pallidum* may have produced a 'booster' effect in the immunity of patients previously treated for syphilis. Because of the possible relationship of other variables, this finding requires further confirmation."

C. J. Hackett

NIYOGI, A. K., PUROHIT, P. B. & TRIVEDI, S. R. **Some Aspects of the Epidemiology of Syphilis and its Prevention.** *J. Indian Med. Ass.* 1959, Oct. 1, v. 33, No. 7, 276–83. [28 refs.]

These authors investigated 1,919 antenatal patients in 3 hospitals in Baroda by means of the Kahn test (repeated if positive) and by visits to the homes of a few of them; positive reactions occurred in 72 (3·5%). Far the largest numbers fell into the lowest socio-economic group, illiteracy was not a factor but most husbands were in the lower occupation groups; the age of the patient was not significant but the greater the number of pregnancies the higher the number of positives; abortions, still-births and infant deaths were also roughly proportional to the number of pregnancies. Of 80 sero-positive persons (72 wives and 8 husbands) 77 were in the latent and 3 (mothers) in the secondary stage of syphilis; proved cases of non-venereal transmission of syphilis were very few; sources of infection were difficult to find.

The incidence of sero-positivity is compared in a table with 11 other places in different parts of the world. Dakar, Madras and Ceylon show the highest figures, Israel, Denmark and France the lowest, Baroda occupying an intermediate position.

A test of voluntary blood donors showed positive rates of 6·8% in males and 3·2% in females.

The trend has been steadily downward from 1956–1958; the high rate is attributed to licensed brothels and epidemiological studies are needed to discover reservoirs of infection.

The authors point out that a positive Kahn test does not necessarily mean syphilis [indeed biological false positive reactions are by no means uncommon in tropical countries].

Results are set out in 14 tables. *T. E. Osmond*

BERG, J. M. & KIRMAN, B. H. **Syphilis as a Cause of Mental Deficiency.** *Brit. Med. J.* 1959, Sept. 12, 400–404. [11 refs.]

The incidence of mental deficiency in syphilitic children has been variously estimated, some figures reaching 19% but it does not follow necessarily that the mental deficiency was caused by syphilis in all cases.

These authors investigated 1,900 mentally defective patients over a period of 12 years and found 12 cases where serum tests for syphilis were consistently positive, where there were clinical signs of syphilis or where there was a history of syphilis in the patient or the mother; 7 of these 12 definitely and 1 probably had congenital syphilis and in 4 there was a history of maternal syphilis; details of 10 are given in 2 tables and of 2 fully in the text.

The diagnoses were taboparesis 3, meningovascular syphilis 2, congenital syphilis with mental defect 3, history of maternal syphilis 4.

Thus if in all 12 mental deficiency was caused by syphilis the incidence would be 0·6%, while if only those with definite congenital syphilis are accepted, it would be 0·2%.

All the evidence suggests that syphilis causes mental deficiency only in the general paralytic and meningovascular forms.

Congenital syphilis is now rare in Britain and syphilitic mental deficiency should disappear if good antenatal supervision is maintained. *T. E. Osmond*

ENG, J. **Serological Tests in Long-Standing Congenital Syphilis. A Case of Long-Standing Congenital Syphilis with only Traces of Antibodies in both the Standard Tests for Syphilis (STS) and the *Treponema pallidum* Immobilization Test (TPI).** *Brit. J. Venereal Dis.* 1959, Dec., v. 35, No. 4, 238–40. [11 refs.]

Several extracts from the literature are quoted where the ordinary serum tests for syphilis (STS) were positive or weakly positive and the TPI negative in late syphilis. The case is reported of a woman who in 1932 at the age of 34 was diagnosed as having keratitis and peripheral choroiditis with perforations of the soft palate; four STS in 1932, 1935, 1937 and 1944 gave positive Meinicke and negative Wassermann (WR) and Kahn tests; treatment in 1932–1933 consisted of 9 injections of bismuth and 4 of neosalvarsan with some potassium iodide. The tests employed were WR and Meinicke with cardiolipin antigen and Wadsworth and Brown's flocculation test (W-Br) with crude antigen. 4 samples of blood were tested in 1958–9; all 4 WR's were negative, 2 Meinicke's were weakly positive and 2 negative and only 1 W-Br was weakly positive. 3 of the TPI's were weakly reactive and 1 negative; this test was repeated 10 times on 2 specimens; in 1 all treponemes were immobilized and in 9 only partial immobilization was noted.

The author discusses the possibility of technical errors in the STS and TPI or the weak STS being false reactions. He thinks more research is needed into the question of the TPI being less sensitive than STS in late syphilis. [In the early days of the Wassermann and flocculation tests it was not very uncommon to get negative reactions in well established cases of late syphilis, presumably because the patient's tissues produced little antibody.] *T. E. Osmond*

OLANSKY, S. & MCCORMICK, G. E., Jr., with the tech cal assistance of Jane MAHALEY. **Experien with the Fluorescent Treponemal Antibody T for Syphilis (FTA Test).** *Arch. Dermat.* 19 Jan., v. 81, No. 1, 59–63, 4 figs. Discussion 63–

To carry out this test, 0·01 ml. of a suspension dehydrated lyophilized treponemes is placed in ea of 2 circles 1 cm. in diameter cut on a glass slide a allowed to dry; 0·03 ml. of a 1/5 dilution of the t serum is added to each and rotated for 30 minu at 100 r.p.m. at 37°C.; the circles are rinsed w buffered saline, the slide blotted dry with filter pa and 0·03 ml. of fluorescein conjugate placed on e smear and the specimen rotated as before; a co glass is applied with mounting medium and the sli examined (at once or after keeping in a refrigera with a Reichert microscope fitted with a 20-watt ul violet-light source. The fluorescein conjugate is a human-globulin tagged with fluorescein isothiocyan

189 sera were tested in parallel by the VDRL s test, Kolmer-Reiter protein test (KRP) and the F test; 96 were reactive and 36 non-reactive with al tests; 20 were non-reactive with VDRL but reac with the other 2; this is not unexpected since VD returns to negative earlier than treponemal tests; 5 w reactive with FTA only suggesting that FTA and give similar results; 17 were reactive with VDRL c and were considered biological false positive reactio 9 were negative with KRP and positive with the o 2—possibly false negatives with KRP; 6 were nega with FTA but positive with the other 2 and v possibly false negatives or technical errors.

It is believed that FTA measures the same antib as TPI and might replace it if further experience b out the claims made for it.

In the discussion which followed doubts w thrown on the specificity of FTA and it was ag that more experience of the test was needed. 4 fig show percentage results with a variety of tests on sera from early syphilis untreated, 232 from treated syphilis, 74 from diseases other than syp and 29 from leprosy patients.

[It is not clear whether sera were inactivated be being tested.] *T. E. Osmon*

NIELSEN, H. A. & METZGER, M. **Incidence of *ponema pallidum* immobilizing Antibody in R bit Immune Sera against Various Types Micro-Organisms and Viruses.** *Brit. J. Vene Dis.* 1959, Dec., v. 35, No. 4, 241–4. [15 refs.

"539 immune sera against various micro-organ and viruses including various serological types of genera and species selected were examined for mobilizing antibody against *T. pallidum* (Nic strain) in the *T. pallidum* immobilization Immobilizing antibody was not demonstrated in of these sera."

BEERMAN, H., NICHOLAS, L., SCHAMBERG, I. L. & GREENBERG, M. S., with the collaboration of T. GUTHE & C. J. HACKETT. **Syphilis. Review of the Recent Literature.** *Arch. Intern. Med.* 1960, Jan. & Feb., v. 105, Nos. 1 & 2, 145–67; 324–40. [175 refs.]

SCHWIMMER, B. & HENDERSON, N. D. **Synnematin B in the Treatment of Syphilis and Gonorrhoea. A Preliminary Report.** *Brit. J. Venereal Dis.* 1959, Dec., v. 35, No. 4, 258–9. [10 refs.]

This antibiotic [this *Bulletin*, 1958, v. 33, 462] is produced by the mould *Cephalosporium salmosynnematum* strain 3590 A, is related to penicillin, is inactivated by penicillinase, has a very low toxicity and appears to have no sensitizing properties; it is active against a wide range of organisms including treponemata and *Neisseria*. These authors tried it out in the treatment of 1 case of florid secondary syphilis and 5 cases of acute gonorrhoea; the dosage was 300,000 units every 6 hours for 3 days for the former and 1 injection of 300,000 units for the latter.

Dark ground examination from a sore was negative after 16 hours and lesions first showed a local Herxheimer reaction and then tended to involute rapidly; signs and symptoms of gonorrhoea cleared rapidly in all 5 cases but 1 patient was presumably reinfected after 26 days. No side-effects were seen.

This antibiotic should be useful in treating patients sensitive to penicillin if the above results are confirmed.

T. E. Osmond

HILTON, A. L. **Treatment of Gonorrhoea with P.A.M. and Probenecid.** *Brit. J. Venereal Dis.* 1959, Dec., v. 35, No. 4, 249–51.

Because of the growing resistance of gonococci to penicillin this author decided to treat gonorrhoea patients with a single injection of 1·2 mega units of PAM accompanied by 0·5 gm. of probenecid [this *Bulletin*, 1957, v. 32, 661] orally every 6 hours for 24 hours. This was found to give serum penicillin levels of 0·15–4·8 μ/ml. (average 1·27 μ/ml.) 21–30 hours after injection.

64 patients including 34 white males, 13 white females and 17 coloured males were treated on this schedule; 58 were followed for 7–70 days; there were no apparent failures but 5 developed non-gonococcal urethritis and 8 (7 coloured males) were reinfected. Side-effects were more marked in females, 4 complaining of burning and soreness of the throat, 2 men complained of nausea, 1 of a rash and 1 of a generalized penicillin sensitivity eruption.

The cost is estimated at 3s. 4d. [per patient] compared with chloramphenicol 7s. 0d., oxytetracycline 10s. 4d. and streptomycin 1s. 2d.

A further 57 male patients have been treated successfully but 2 out of 18 females have been failures.

T. E. Osmond

GJESSING, H. C. **Increasing Failure Rate after using the Same Preparation and Dosage of Penicillin in the Treatment of Gonorrhoea.** *Brit. J. Venereal Dis.* 1959, Dec., v. 35, No. 4, 256–7.

It is generally agreed that for the cure of gonorrhoea bigger doses of penicillin are required now than formerly. This author reports that in the period 1949–50 among 321 patients the failure rate was 2·2–2·9%; in 1950–52 the respective figures were 326 and 2·8–3·7 and in 1952–55 they were 391 and 3·0–4·1; 3 different preparations of penicillin were employed in the same dosage, *i.e.* duracillin, duracillin AS and procaine-penicillin G Novo. When this last was employed over succeeding periods the relapse rate rose from 2–2·6 up to the end of 1954 to 8·6–11 up to the end of 1957.

Admittedly it is often difficult to distinguish between reinfection and relapse but the latter usually occurs within 1–2 weeks after treatment and reinfection is assumed if the patient admits sexual intercourse and symptoms appear at the appropriate time.

The author thinks that even small amounts of alcohol taken during the first week after treatment favour relapse [though how this should be is not clear if all gonococci have been killed by penicillin in the first 24–48 hours as is generally assumed].

No doubt the increased failure rate is due to increased resistance on the part of the gonococcus and the author now uses double the dosage employed formerly.

T. E. Osmond

THOMSON, G. M. **Treatment of Male Gonorrhoea with a Chlortetracycline-Sulphonamide Combination.** *Brit. J. Venereal Dis.* 1959, Dec., v. 35, No. 4, 254–5.

Owing to the increasing risk of sensitivity reactions with penicillin this author treated 138 male patients in Hong Kong suffering from early gonorrhoea with a chlortetracycline-sulphonamide combination; each patient was given 2 capsules of 250 mgm. of aureomycin plus 0·5 gm. Lederkyn (sulphamethoxypyridazine) at once and 2 capsules of aureomycin to be taken 8 hours later; patients were seen again 2 and 7 days later.

Of the 138 patients 101 were cured (92·6%), 8 were failures or relapses and 29 defaulted; follow up showed "no such address", 11; "no such person", 16; "moved away", 2. No side-reactions were noted and only 2 patients showed evidence later of non-gonococcal urethritis; the cost of treatment was 10s. 0d. per person.

T. E. Osmond

ROSEDALE, N. **Female Consorts of Men with Non-Gonococcal Urethritis.** *Brit. J. Venereal Dis.* 1959, Dec., v. 35, No. 4, 245–8.

This author investigated 150 females who were the consorts of male patients suffering from non-gonococcal urethritis (NGU); 140 were white and 10 coloured; 102 fell into the 20–30 age-group; 73 were

married [presumably wives of the patients] 75 single and 2 widowed; 86 had no symptoms, 55 had a slight discharge and 9 had dysuria. On routine examination 99 appeared normal, 20 had cervicitis only, 13 vaginitis only and 18 had both; *Trichomonas vaginalis* were present in 18 (but in only 2 of the men).

Treatment of the females comprised (1) local—pessaries, (2) streptomycin 1 gm. daily for 3–5 days, (3) 1,200,000 units penicillin, (4) aureomycin, oxytetracycline or tetracycline 0·25 gm. 4 times a day for 4–5 days, (5) streptomycin 1 gm. + sulphonamide 1 gm. 4 times a day for 5 days.

The relapse rate among males varied from 7·1 to 50% being lowest where the female was treated according to schedules 4 and 5; 21·6% of all males relapsed and 33% of those whose consorts were not treated relapsed.

[No very clear conclusions can be drawn from the above but it does seem that treatment of the female makes very little difference; however, since roughly half the male patients had sexual intercourse with women other than their wives, reinfection seems just as probable as relapse.] *T. E. Osmond*

LEACH, W. **Treatment of Non-Gonococcal Urethritis with Sigmamycin. A Controlled Method of Investigation.** *Brit. J. Venereal Dis.* 1959, Dec., v. 35, No. 4, 223–30, 6 figs.

This long and well documented article records the results of treating non-gonococcal urethritis (NGU) with sigmamycin according to 2 dosage schedules with suitable controls; a double-blind method was employed on 200 patients. Results are set out in the text and in 6 figures and 16 tables. The dosages were 100 mgm. every 6 hours for 4 days and 500 mgm. every 6 hours for 5 days [but there appears to be no certainty that all these doses were taken]; progress was assessed by the appearance of the early-morning urine weekly for 8 weeks.

The patients were mostly between 20 and 30 or 30 and 40, almost equal numbers were single or married, the chief symptom [? sign] was urethral discharge (93·5%) and 48% had dysuria; 68·5% had had symptoms for 6 days; the contact was usually a girl friend or fiancée who usually had non-gonococcal cervicitis; the incubation period averaged 11·7 days; 38% of patients gave a history of previous urethritis, gonococcal or non-gonococcal.

Results showed success rates at the end of 8 weeks of 58·5% in the low dose group and 73% in the high dose group compared with 49·5% and 54·5% respectively in the control groups; recurrences occurred in 24·5 and 20% of the treated groups and in 10·5 and 6·5% of the control groups. Causes of recurrence were sexual intercourse 19%, alcohol 42% and activity 3%; the chief complication was prostatitis; side-effects were negligible; the main organisms involved were staphylococci, *Proteus* and coliforms.

It is concluded that sigmamycin (tetracycline hydrochloride + oleandomycin phosphate) does not show synergism but is useful in the treatment of NGU if given in adequate dosage. *T. E. Osmond*

JELINEK, G. **Treatment of Non-Gonococcal Urethritis A Further Report on its Efficiency and Cost** *Brit. J. Venereal Dis.* 1959, Dec., v. 35, No. 4 252–3.

This author treated 3 groups of patients sufferin from non-gonococcal urethritis according to 3 differer schedules which were as follows:

(1) 1 gm. streptomycin sulphate (streptaquaine) b injection with 0·5 gm. Lederkyn (sulphamethoxy pyridazine) twice daily for 5 days [? orally].
(2) 1 gm. streptomycin sulphate with 0·5 gm. Lederky once daily for 5 days.
(3) 1 gm. Achromycin "V" (tetracycline buffere with citric acid or sodium metaphosphate) in divided doses daily for 4 days.

With schedule 1 of 56 patients 5 defaulted, 82·3% were cured and the cost was 6s. 10d. With schedule the respective figures were 79, 14, 75·3 and 4s. 2 With schedule 3 the figures were 32, 6, 61·5 and 23s.

In a previous series streptomycin with sulphatria (25 gm.) gave a cure rate of 78% [this *Bulletin*, 195 v. 33, 123] and Achromycin 4 gm. a rate of 62%.

It is concluded that a cheap, simple and safe dru combination should be preferred, at first at any rat to the more expensive drugs. *T. E. Osmond*

CSONKA, G. W. **Treatment of Non-Specific Urethrit with Tri-Acetyl-Oleandomycin.** *Brit. J. Venere Dis.* 1959, Dec., v. 35, No. 4, 262–3.

This author treated 22 patients suffering from ear non-specific urethritis, 12 with this drug and 10 wi a placebo (lactose powder) as a double-blind ther peutic trial; 3 of the 12 and 8 of the 10 were appare failures after 6–7 days; these 11 were re-treated wi oxytetracycline 250 mgm. orally 4 times a day for days; the control group responded much the bette Cultural tests for pleuropneumonia-like organism before and after treatment indicated that these org nisms were or were not present independently of t outcome of the disease.

The apparent treatment success rate was about 75 compared with 20% of the control group.

T. E. Osmond

WILLCOX, R. R. **Treatment of Non-Gonococcal Ur thritis with Tri-Acetyl-Oleandomycin.** *Brit. Venereal Dis.* 1959, Dec., v. 35, No. 4, 264–5.

This author treated 100 patients suffering from no gonococcal urethritis with this drug, known as Evr mycin; 30 were negroes from the West Indies or We Africa and of the others 53 were from the Unit Kingdom and the remainder from 9 other countrie 68 were single, 31 married and 1 separated; only had not had a previous venereal incident; the disea had been present for 1–28 days or more and the inc bation period also varied from 1–28 days. Treatme consisted of 1 250 mgm. capsule orally 4 times a d for 6 days and where possible observation extend over 12 weeks.

Of 85 followed up, 23 (27·1%) needed retreatment within 3 months; the retreatment rate was 31·8% for negroes and 25·4% for the others.

7 patients were considered to have been reinfected and 6 to have contracted gonorrhoea within 3 months. Side-effects, rectal soreness, irritation or burning occurred in only 3 patients.

The success rate of 72·9% suggests that this drug is useful in the treatment of non-gonococcal urethritis. *T. E. Osmond*

Ghosh, S. & Ghosh, R. **Donovanosis treated with Erythromycin Parenterally. Report of First Case.** *Brit. J. Venereal Dis.* 1959, Dec., v. 35, No. 4, 260–61.

The usual treatment of granuloma inguinale (Donovanosis) in the recent past has been streptomycin; these authors report a case treated with Ilotycin erythromycin 100 mgm./2 ml. intramuscularly twice daily for 15 injections. On examination the patient showed erosion of the prepuce, swollen and oedematous penis, thickened skin of scrotum and a warty granulomatous swelling in the perineum and right groin; the VDRL reaction was positive, Q.T. 1:4 negative [it is not clear what this means], Meinicke-Kahn reaction II positive and Price's precipitation reaction with cardiolipin antigen weakly positive; Donovan bodies were seen in a biopsy specimen. [The significance of the serum tests for syphilis is not explained.] Under treatment the lesions healed rapidly; two small sinuses in the groin were treated [with ?] and penicillin and streptomycin injections with a local application were given after 12 days [but the reason for these is not stated]. *T. E. Osmond*

GENERAL INFECTIVE DISEASES

The order in this section is:—**General; Hospital and Other Cross Infections; Coccal Infections; Bacterial Infections; Virus Infections.**

GENERAL

Zourbas, J. Calendrier des vaccinations. **[Inoculation Programme in Children in Relation to Age]** *Ann. Inst. Pasteur.* 1959, Dec., v. 97, No. 6, 794–817. [50 refs.]

This paper is divided into two sections:

I. *Epidemiology.* Examination of problems relating to the incidence of infectious diseases such as diphtheria, influenza, tetanus, whooping cough, poliomyelitis and tuberculosis together with a consideration of the special risks of different age-groups.

II. *Immunology.* Various problems relating to immunity in the infant and the young child are discussed. The immune response to combined prophylactics is also considered, together with the optimum age of the child for inoculation of the various vaccines. The author then produces an inoculation programme for the immunization of children from birth (BCG in special cases) up to the age of 10 years for protection against whooping cough, diphtheria, tetanus, smallpox, poliomyelitis and the enteric fevers. In general it may be said that the recommended programme is not significantly different from the one recommended in Great Britain. Combined prophylactics are favoured and although simple pertussis vaccine at 3 months would seem to be preferred it is also indicated that combined pertussis, diphtheria and tetanus prophylactic can be employed at that age. The possibility of combining poliomyelitis vaccine with these other 3 immunizing agents is also discussed. *H. J. Bensted*

Chevé, J., Girard, O., Nicol, L., Amoureux, G. & Zourbas, J. Vaccination anti-diphtérique, anti-tétanique, anti-coquelucheuse. **[Vaccination against Diphtheria Tetanus and Whooping Cough]** *Ann. Inst. Pasteur.* 1959, Dec., v. 97, No. 6, 818–34, 8 figs. [16 refs.]

This is a consideration of the immune response of young children to various inoculation procedures with combined prophylactics against diphtheria, tetanus and whooping cough based on evidence obtained from examinations of the sera obtained from children attending inoculation clinics in Paris. The main object of this survey appears to have been to determine whether the use of this combined prophylactic for young children at the age of 3 months resulted in the production of antibody levels which could be considered satisfactory. These preliminary studies indicate that the results obtained are statistically significant but further work is in progress and will be reported later. *H. J. Bensted*

Faerber, K. P. & Seelemann, K. Beobachtungen über die Verträglichkeit eines neuen kombinierten Diphtherie-Tetanus-Poliomyelitis-Impfstoffes. **[Observations on the Toleration of a New Combined Prophylactic against Diphtheria, Tetanus and Poliomyelitis]** *Öffentl. Gesundheitsdienst.* Stuttgart. 1959, v. 21, No. 8, 309–15. [10 refs.]

The prophylactic tried out was a preparation put out by Behring which contains in 1 ml. 50 international

units of diphtheria and of tetanus toxoids together with 0·5 ml. of a mixture of the 3 recognized polioviruses which have been inactivated with formalin. In Oberhausen 1,624 children received 2 injections. In Hamburg 2,181 also had 2 injections.

There were no severe reactions and less than 1% of general reactions. *J. W. McLeod*

HOSPITAL AND OTHER CROSS INFECTIONS

VOGELSANG, T. M. Laboratorie—undersøkelser over forekomsten av patogene stafylokokker i hospitalsmiljø. [**Laboratory Investigations of the Occurrence of Pathogenic Staphylococci in a Hospital Environment**] *Tidsskr. f.d. Norske Laegeforening.* 1959, May 1, v. 79, No. 9, 517–23, 4 figs. [48 refs.]

In charge of the Microbiological Department of Gade's Institute in Bergen, Professor Vogelsang has since 1949 been publishing singly or in conjunction with his colleagues a series of reports on the behaviour of staphylococci in hospital in response to penicillin medication [see, for example, this *Bulletin*, 1954, v. 29, 666, 772, 773, 994, *bis*; 1959, v. 34, 169]. This, his latest report, goes back to 1945 when penicillin was first tested in Bergen. An examination in 1946–47 and another in 1949–51 of the patients in Haukeland Hospital failed to show any increase in the number of penicillin-resistant staphylococci on their admission. A new examination in 1951–52 showed a slight increase on admission and a marked increase on discharge from hospital. Next year about one-half of the strains isolated from patients on their discharge from a children's hospital were penicillin-resistant. In 1953, on the medical side of Haukeland Hospital, 81% of the strains cultivated from the medical and nursing staff were penicillin-resistant. Of late, antibiotics other than penicillin may have partially replaced it and thereby discouraged the growth of penicillin-resistant strains. Tests carried out in 1958 by VOGELSANG and HAALAND with this possibility in mind have been reported on in 1959 [this *Bulletin*, 1960, v. 35, 283]. The introduction of a new method for resistance determination has, however, interfered with a comparison of the latest with earlier figures.

The measures Vogelsang advocates for tackling the problem hinge largely on early diagnosis promptly followed up by isolation of the offenders, whether they be patients or members of the hospital staff. The latter could be given leave of absence, for experience has shown that many persons are intermittent carriers, with a good chance to get rid of an epidemic strain in the upper respiratory tract during residence outside hospital. *Claude Lillingston*

VOGEL, R. A., TROTTER, Y. J., SHINABERGER, J. H. & MCCROAN, J. E. **The Genesis and Spread of a Hospital Staphylococcal Epidemic on an Adult Medical Ward.** *New England J. of Med.* 1959, Dec. 24, v. 261, No. 26, 1301–9, 6 figs. [29 refs.]

Surveillance for staphylococcal infection had been in progress in a 300-bed Veteran's hospital for 10 months when a sudden change in the prevalent phage type c staphylococcus was observed. Previously the dominan types were 7/77, VA4 [83] and 53/77. In Septembe and October 1957, 5 strains of type 52/52A/80 wer isolated. In January and February 1958 there was sharp increase in staphylococcal infection due to th 52/52A/80 strain. At first the cases were mostly lun infections complicating influenza but subsequently a epidemic of skin infections was seen. There were 2 patients with respiratory tract infections, 14 of whor died, with the staphylococcal infection regarded as major factor leading to death in 11. 38 patients ha skin infections. There was some evidence that par at least, of the ward-to-ward spread was due to patient who had an extensive staphylococcal infectio of the skin. Only 1 of 153 members of the hospit staff carried the epidemic type just before the ep demic, and only 7 were detected near its end. Th infection was apparently spread from the hospital in one man's family leading to 5 cases of respirato infection with 2 deaths.

Control measures included isolation of infecte patients, cleansing of contaminated rooms and steriliz tion of fomites, etc. *R. E. O. Williams*

HURST, Valerie. **Transmission of Hospital Staphyl cocci among Newborn Infants. I. Observatio on the Contamination of a New Nurser** *Pediatrics.* Springfield, Ill. 1960, Jan., v. 25, No. 11–20, 2 figs. [30 refs.]

A comparison was made of the rate of acquisiti of *Staphylococcus aureus* by infants in a matern unit before and after the unit's transfer to a n hospital in which the physical facilities, as to bc space and equipment, were greatly improved. Na swabs were taken from the infants daily from the 2 day of life until their discharge, apparently at the 6 to the 8th day. No difference was found in t average staphylococcal carrier rate, which was 40% the old and 43–44% in the new nursery. In one-h of the new hospital the nurses wore masks, but t babies in this unit had as high a carrier rate as the in the other. The infants continued to become infect with the same phage types of staphylococci in the n nursery; these types differed from those carried by t nurses. Air contamination with staphylococci appea soon after the transfer of the infants to the n nursery and continued at much the same level as the old nursery, despite the fact that the new one w supplied with 15 air changes per hour of fresh a It seemed likely that the rapid contamination of new nursery was due to transfer to it of babies wh umbilicus was already colonized by staphyloco The results are thought to support the view that a borne transfer of staphylococci is important, and t nasal colonization, and, by inference, sepsis, will o be prevented by proper rooming-in units with air loc [But the evidence that the transfer was in fact by a borne particles, rather than by indirect contact, d not appear to be strong.] *R. E. O. William*

SIMPSON, K., TOZER, Rosemary C. & GILLESPIE, W. A. **Prevention of Staphylococcal Sepsis in a Maternity Hospital by means of Hexachlorophane.** *Brit. Med. J.* 1960, Jan. 30, 315–17, 2 figs.

The acquisition of staphylococci in the nose and on the skin of newborn babies was observed by swabbing the nose, perineum, groin and umbilicus at the 2nd, 4th, 6th and 10th day of life. Before the introduction of hexachlorophane 80% of babies had *Staph. aureus* in the nose by the 10th day; 50% had the cocci on the umbilicus or groin by the 4th day but the proportion was only 20% at the 10th. For 6 months all the babies in 1 nursery had hexachlorophane dusting powder applied to the cord stump and front of abdomen each time the napkin was changed. The maximum nasal carrier rate was just over 50% and the rate for the skin areas never rose above about 16%. Later the same powder was used for the whole of the baby's trunk with a further slight fall in the staphylococcal colonization.

The percentages of infants developing skin sepsis under the 3 regimens were 5·2, 2·0 and 0·9, respectively. In another nursery, kept as a untreated control the rate over the whole period was 7·3%.

The control nursery had to be closed for a period because of an outbreak of pemphigus; the nursery was disinfected and bedding changed. On reopening, the infants were rapidly recolonized by new staphylococci, presumably from staff carriers.

An attempt was made, in the control nursery, to reduce the degree of contact between nurses and infants by the use of wheeled cots and other measures. There was no effect on the incidence of sepsis and no more than a doubtful effect on the acquisition of staphylococci in the nose.

[For an earlier study, see this *Bulletin*, 1959, v. 34, 311.] *R. E. O. Williams*

FARRER, S. M., RUSSO, R., BAVARA, Camille & WERTHAMER, S. **Surveillance and Control of Staphylococcic Infections in a Maternity Unit.** *J. Amer. Med. Ass.* 1959, Oct. 24, v. 171, No. 8, 1072–9, 2 figs. [20 refs.]

Between September 1957 and January 1959, 26·2% of the live births in a hospital in Lakewood, New Jersey, were followed by sepsis in the infant (211 in all) or mother (30). These rates were obtained by a telephone survey conducted 6 weeks after the mothers and babies left hospital; a follow-up rate of 81% was achieved. There were 2 periods of high prevalence with peak rates of infection of 50–60%; in the non-epidemic periods the rate was about 7%. Most of the lesions in both mothers and babies were cutaneous; 5 mothers and 3 babies developed abscesses of the breast or other sites. Of 63 staphylococcal strains from lesions 65% were type 80/81. This type was also found, at the first peak of the epidemic, in the nose of 5% of the babies at discharge when 5–6 days old. 16 members of the staff were found to be persistent carriers of type 80/81.

To control the epidemic, staff carriers were transferred to other duties or, in the case of doctors, subjected to special precautions; all healthy babies were discharged after 3 days; breast feeding was discouraged; aseptic routines were improved. There was a rapid decline in the infections to a low level which persisted for 4 months but was followed by a second severe epidemic. The source of this outbreak was not discovered [and no bacteriological studies of this stage are reported]. Compulsory "rooming-in" [no details], painting of the cord stump with triple dye, and administration of gamma globulin were instituted and the infection rate dropped sharply and continued low even when the triple dye and gamma globulin were abandoned. [Nevertheless, without further study, the part played by rooming-in in controlling the outbreak cannot be properly assessed] *R. E. O. Williams*

WILLIAMS, R., WILLIAMS, E. D. & HYAMS, D. E. **Cross-Infection with *Pseudomonas pyocyanea*.** *Lancet.* 1960, Feb. 13, 376–9, 1 fig. [17 refs.]

During 1959 there appeared to have been an increase in the incidence of infection with *Pseudomonas pyocyanea* at the Postgraduate Medical School, London and in 1 ward 5 patients died with pseudomonas infections, 3 with septicaemia, 1 with bronchopneumonia 1 with diarrhoea. Transmission of infection was thought to be through the air and patients with infected sputum are postulated as a probable source. Judged from antibiotic sensitivity patterns there appeared to be several different strains in circulation.

All the patients had had previous treatment with broad-spectrum antibiotics and with corticosteroids; 4 had some blood disorder. It is suggested that patients with leucopenia, who are at special risk, ought to be nursed in isolation. *R. E. O. Williams*

COCCAL INFECTIONS

The order in this section is:—*Staphylococcus, Streptococcus, Neisseria, Others.*

ŠEBEK, V., SCHUBERT, J. & JOHANOVSKÝ, J. Možnosti imunoprevence stafylokokových nákaz matek a novorozenců. IV. **[The Possibility of Immunoprevention of Staphylococcal Infections in Mothers and Newborn Infants]** *Časopis Lékařů Českých.* Prague. 1959, Sept. 18, v. 98, No. 38, 1181–8. [15 refs.] English summary.

An investigation has been made of the effect of the immunization of expectant mothers with staphylococcal toxoid upon the incidence of staphylococcal infections after birth. Staphylococcal toxin was inactivated with formaldehyde and the toxoid was mixed with aluminium hydroxide gel and diluted in buffered saline. It was administered in 1 or 2 doses given 8 and 4 weeks before the expected date of delivery; 250 women

were treated in all, and in most instances satisfactory antitoxin and antileucocidin titres were attained. In the 3 months after delivery staphylococcal infections (pyrexia, mastitis) were observed in 14 (8·6%) of 163 women given 2 doses of toxoid and in 11 (13·5%) of 81 given 1 dose, compared with 145 (32·4%) of 448 unimmunized women in a control group. The incidence of staphylococcal infections (umbilical granuloma, conjunctivitis, folliculitis, pemphigus and furuncles) among their infants while in hospital was 12·3% and 9·9% in the 2 treated groups and 30·1% in the control group. *D. J. Bauer*

Bonilla-Soto, O. & Pomales-Lebrón, A. **Variation with Age of Antistreptococcal Antibodies and their Correlation with Antistreptolysin O Titers in Human Sera.** *Proc. Soc. Exper. Biol. & Med.* 1959, Nov., v. 102, No. 2, 337–40, 2 figs. [10 refs.]

Sera from 9 infants at birth (cord blood) and 74 aged 1 to 12 months were examined by gel precipitation against a group A haemolytic streptococcus culture fluid; 331 normal adult sera were also examined. The average number of precipitin bands in the sera of the new born was 2·2; the number dropped to zero in those aged 4–11 months. Adult sera had on average 2·5 bands. In the adult sera there was a correlation between the number of bands and the antistreptolysin titre. *R. E. O. Williams*

Stillerman, M., Bernstein, S. H., Smith, Martha L., Gittelson, S. B. & Karelitz, S. **Antibiotics in the Treatment of Beta-Hemolytic Streptococcal Pharyngitis: Factors influencing the Results.** *Pediatrics.* Springfield, Ill. 1960, Jan., v. 25, No. 1, 27–34, 2 figs. [20 refs.]

Penicillin given orally or intramuscularly was shown to be much superior to erythromycin or tetracycline in the treatment of streptococcal pharyngitis, cure rates being 84% against 48% and 38% respectively. There was no difference in effectiveness of penicillin V, penicillin V potassium and benzathine penicillin G. There was a relapse and failure rate of 15% in spite of penicillin therapy. *A. B. Christie*

Taitz, L. S. & Slone, D. **Treatment of Pneumonia in Children. Use of Oral Penicillin in Out-Patients.** *Brit. Med. J.* 1960, Feb. 6, 398–9.

33 non-white children over 3 months of age, found at an out-patient clinic in Johannesburg to be suffering from mild or moderately severe pneumonia, were treated with phenoxymethyl penicillin (penicillin V) as out-patients. The cases were selected on the basis of presence of dyspnoea with or without physical signs, but with radiographic evidence of consolidation or loss of translucency in the lung fields. Patients with cyanosis or cardiac failure were excluded, and treated as in-patients. The dosage was 200,000 units every 4 or 6 hours for 2–3 days. With this treatment there was evidence that 29 (87%) recovered. Of the 4 oth patients, 2 had a relapse, 1 was found to have whoo ing cough pneumonia, and 1 to have pulmona tuberculosis.

An advantage was the relative absence of relaps due to superinfection with penicillin-resistant organism Out-patient treatment can be the treatment of choi in selected cases of pneumonia. *H. Stanley Banks*

BACTERIAL INFECTIONS

The order in this section is:—*General, Coryn bacterium, Haemophilus, Enteric bacteria, Bruce Pasteurella, Bacillus, Anaerobes, Spirochaetes, Others.*

Jansson, E., Jalava, Liisa & Wager, O. **C Reacti Protein in Bacterial Meningitis.** *Ann. Me Exper. et Biol. Fenniae.* Helsinki. 1959, v. 3 No. 4, 371–6.

A previous study (*Ann. Med. Exper. et Bi Fenniae*, 1957, v. 35, 352) had shown that practical no C-reactive protein (CRP) was to be found in t serum of patients with serous meningitis or paraly poliomyelitis. This paper extends the study to ba terial meningitis in its early stages, when distincti from viral meningitis may be difficult. It concerns subjects with meningitis due to *Streptococcus pneum niae, Haemophilus influenzae, Neisseria meningitid Staphylococcus aureus,* or *Mycobacterium tube culosis,* whose personal and laboratory details a tabulated. The test for CRP was consistently positi in specimens taken on the 1st, 2nd and 3rd da in 10 of the 25 sera examined on the 7th day it w negative. This result contrasts with the consisten negative CRP test found in 50 out of 63 cases serous meningitis; furthermore 8 of the 13 positi subjects in this group had some additional conditi which might have accounted for the presence of CR

Since the test (the appearance of a precipitin ri in a capillary tube) can often be read within an ho of venesection, and since the result becomes positi early and does not appear to be influenced by the u of antibiotics, it is recommended as a valuable aid distinguishing bacterial from "serous" meningit (The antigen used was a commercial anti-CRP rab immune serum from Schieffelin & Co., New York.) *Alan B. Raper*

Dunnet, W. N., Schallibaum, E. M. & Scott, T. **Fatal Diphtheria in the Fully Immunized Chil** [Memoranda.] *Brit. Med. J.* 1960, Jan. 23, 251–

A child 8½ years of age, who had had 2 doses diphtheria prophylactic (APT) in 1950 and a boos dose of TAF in 1956, was admitted on the 4th day disease with tonsillar, palatal, and laryngeal diphther associated with *Corynebacterium diphtheriae mitis* throat swabs. She was given 16,000 units antito

intramuscularly and 80,000 intravenously on admission, and as there was some stridor and cyanosis, tracheotomy was performed. Erythromycin and, later, chloramphenicol were also given. Pneumonia, with consolidated right upper lobe, developed 2 days later, and she died 3 days after admission. Serum electrophoresis had revealed no hypogammaglobulinaemia.

[The authors are evidently puzzled why this apparently immunized child developed such severe diphtheria, and why she developed pneumonia and died so rapidly. It could be argued that her 2 primary prophylactic injections must have been given when she was a very young infant, possibly resulting in relatively weak immunity, and that a booster dose of the weak prophylactic TAF 6 years later might well have been insufficient to boost her immunity to an adequate level. As to the cause of death, the characteristic signs and symptoms of an early death from diphtheritic myocarditis are not mentioned, and the principal cause would seem to have been the pneumonia. Why this did not respond to the antibiotics is not easy to understand, but the tracheotomy might well have been the aggravating, or even the causal, factor in the pneumonia. If tracheotomy in this case could have been avoided (as would seem possible in a child 8½ years old) the result might have been different.]

H. Stanley Banks

Prévot, A. R. Les corynébactérioses anaérobies. [**Infections with Anaerobic Corynebacteria**] *Ergebn. Mikrobiol. Immunitätsf.* 1960, v. 33, 1–48, 6 figs. [Numerous refs.]

Brewster, J. H., Donaldson, S. N. & Logue, A. M. **A Typhoid Fever Outbreak at Ballyreagh, Co. Londonderry.** *Med. Officer.* 1960, Mar. 4, v. 103, No. 10, 133–6, 2 figs.

An outbreak of typhoid fever occurred during July and August, 1959 among persons occupying a popular coastal site for caravans and temporary dwellings at Ballyreagh (Co. Londonderry). There were 29 confirmed cases (16 male and 13 female) all of which were mild. The causal organism was of phage type C1.

There is no water-borne sewage in the area except in some of the permanent dwellings. Dry closets are the rule and although the owners of the site provide trenches for disposal these are not always used and excreta are buried at random or thrown over the cliff at night.

A good account is given of the preventive measures and investigations which were undertaken. The outbreak was limited to persons resident in or who had visited 1 of the several fields which compose the caravan site. The water supply consisted of stand-taps from mains but in addition there are several wells. It is of interest that many of the inhabitants preferred the well water as it was clear and sparkling and better in appearance than the mains supply. The well in the field where the cases of typhoid occurred was proved to be polluted and was almost certainly the vehicle of spread. Several persons who contracted typhoid had also bathed in pools open to excretal pollution and eaten shellfish from the adjoining rocks. In a search for carriers blood samples were taken from 54 persons—residents on the infected site, food tradesmen and milk roundsmen. Ultimately 1 of these, a man, was proved to be a carrier who was a faecal excreter of phage type C1. Cholecystectomy was performed on him and typhoid organisms were isolated from the gall bladder. This man was not at the time resident in the infected district but had ready access to the well.

The immediate steps taken to prevent the spread of the outbreak were entirely successful. Reference is made to the inadequacy of present legislation for the control of caravan sites. *M. E. Delafield*

De Gregorio, M. Episodio di febbre tifoide di origine idrica. [**A Waterborne Outbreak of Typhoid Fever**] *Riv. Italiana d'Igiene.* 1959, Sept.–Oct., v. 19, Nos. 9/10, 530–33.

Alessandria del Carretto is a rural district in Cosenza, Calabria, at a height of 1,000 metres above sea level, with 2,000 inhabitants—mostly peasants and shepherds on a low standard of living. There had been only 2 sporadic cases of enteric fever within the first 7 months of 1958, but 19 cases—an incidence of nearly 1%—occurred in the course of August and September: ages varied from 4 to 62 years.

Suspicion seems to have fallen mainly on certain salad vegetables from a neighbouring town as the cause, but control measures based on this suspicion made no impression on the progress of the epidemic. De Gregorio paid a visit to the area towards the end of September and noticed that the cases came from one neighbourhood where the inhabitants obtained water from an old shallow well, allegedly not for drinking purposes. This well was closed and the epidemic came to an end. All efforts to isolate the specific organism from the well water, even with enrichment and selective culture, proved negative. A strain of *Escherichia coli* Type I was present in 0·10 cc. of samples drawn from this well. *J. Cauchi*

Bernard, J. G. & Jauneau, A. Fièvre typhoïde et vaccination. [**Typhoid Fever and Vaccination**] *Rev. d'Immunologie.* 1959, July–Sept., v. 23, No. 4, 276–93, 3 graphs. [33 refs.]

This paper is concerned with a reconsideration of the effectiveness of TAB inoculations in protecting against the enteric group of fevers. The evidence considered is not provided by any system of properly controlled trials, but by an analysis of morbidity figures from the French Army over various periods. It is of interest to note that the young recruit in the French Army receives for his primary immunization, 3 doses of TABDT (typhoid-paratyphoid vaccine combined with diphtheria and tetanus prophylactics) with intervals of 15 days between the injections; 10–14

months later he is given a single booster dose of TABDT.

Different vaccine preparations are considered and also the value of antibiotic therapy, but the general conclusion is that antityphoid vaccination is an important prophylactic procedure for populations exposed to special risks of infection. An example of the figures given to support such a conclusion are as follows:—

			Morbidity
Total nos. at risk		2,327	
Cases of typhoid	158		6·9%
Completely immunized		2,126	
Cases of typhoid	137		6·4%
Incompletely immunized		126	
Cases of typhoid	10		7·9%
Non-vaccinated persons		75	
Cases of typhoid	11		14·6%

The figures could not be accepted for statistical analysis as they were not obtained in any properly controlled trial and their significance is therefore doubtful. *H. J. Bensted*

DEWAR, J. **A Hospital Outbreak of Paratyphoid Infection.** *Health Bull.* (Issued by the Chief M.O., Dept. of Health, Scotland.) 1959, Oct., v. 17, No. 4, 71–2.

A child of 2 years was admitted to a ward block in a 70-bed hospital (containing cubicles for infectious diseases as well as a ward for the chronic sick) from which she had been discharged after treatment for broncho-pneumonia 13 days previously; she was now found to be suffering from paratyphoid B fever. 7 days later a woman of 92 in the section of the ward block for the chronically sick had mild pyrexia and diarrhoea for 1 day, and *Salm. paratyphi B* of the same phage type was found in her stools. No source of the child's infection was discovered in her family circle or elsewhere outside the hospital. Accordingly the whole of the nursing, domestic, and catering staff of the hospital and all of the patients had their stools examined, and the same organism was recovered from 2 of the nursing staff, 3 chronically sick and 2 other patients; all of these 7 were symptomless excreters, and it was impossible to say which of the 9 infected persons was the primary source. This is a good example of the extent to which paratyphoid infection can spread in an institution with the minimum of symptoms. *H. Stanley Banks*

BRODIE, J., BRUNTON, D. P. & CHAMBERS, W. **Observations on an Institutional Outbreak of Paratyphoid Fever in Aberdeen, 1958.** *Health Bull.* (Issued by the Chief M.O., Dept. of Health, Scotland.) 1959, Oct., v. 17, No. 4, 72–3.

This is an interesting example of an institutional outbreak of paratyphoid fever in 1958 traced to an unknown chronic carrier employed in the kitchen of the institution. 20 persons (residents and staff) were discovered to be harbouring *Salm. paratyphi B* of phage type 2, but only 3 of these had symptoms; t organism was recovered only in the 5th specim examined in 1 woman, and only in the 6th and specimens respectively in 2 children. A female resid kitchen worker aged 67 admitted a past history symptomless paratyphoid infection while employed cooking duties in a Dundee hospital in 1942 when th was a major epidemic of paratyphoid fever; after months' observation there, during which time she mained a carrier of phage type 2 paratyphoid B, she h "walked out" of the hospital and disappeared. Su sequently she had been employed as a cook in vario households but no cases of paratyphoid attributa to her during that period were traced. She was co sidered to be the cause of the present outbreak, wh comprised 3 cases and 17 carriers.

All the infected persons were treated with chlora phenicol for 10 days, and in some cases also with c streptomycin; when the infection was not clea after this treatment, further courses of chloramphenic streptomycin, and neomycin or aureomycin were giv the organism was tested for sensitivity to all these an biotics. The average time for clearance was 12 wee and all were ascertained to be clear during a furt 6 weeks of observation except the original chro carrier and one invalid woman aged 87 years; former, who remains a chronic carrier in spite cholecystectomy, has retired from work and lives alo and the latter, also a chronic carrier, remains un close observation in the institution.

H. Stanley Bank

WATKINS, J. F. *Salmonella paratyphi* **BO Agglutin Levels in Paratyphoid B Fever.** *J. Roy. Ar Med. Corps.* 1959, Oct., v. 105, No. 4, 167– 1 fig.

An outbreak of infection due to *Salmonella pa typhi B* in the Middle East in 1952 provided opportunity for the study of the O-agglutinin respo to this infection in inoculated subjects. The mate used and the methods employed were carefully c trolled and it is reported that in 44 proved cases infection with paratyphoid B the examination "paired sera" (acute and convalescent specime failed to show a significant rise in agglutinin-titre more than one-fifth of the cases and 43% showed change in titre of the O-agglutinins. The author c cludes that "routine BO agglutination on single paired sera was of little value in diagnosis in outbreak".

[The examinations reported here were carried with care and with proper controls and there is reason to doubt the accuracy of the work, but th are certain aspects of paratyphoid B infections are sometimes overlooked. The incubation period be short and the clinical picture that of a mild ente rather than an enteric fever and the author indic that his cases were of this type. It is character of such outbreaks to find a significant proportion persons excreting paratyphoid organisms without sh ing any signs of illness as in many outbreaks

infection due to *Salm. typhi-murium*, where the epidemiological pattern and, apparently, the pathological process are very similar. Such mild transient infections cannot be expected to induce any marked somatic antibody response and it is a common experience in retrospective serological investigations of food-poisoning outbreaks to find that very few of those involved have significant O-agglutinins to the organism responsible. While it is important in epidemiological studies to identify every person found to be excreting the epidemic organism, when the infection is due to *Salm. paratyphi B*, the inclusion of all excreters as cases of enteric fever may lead to misunderstanding in some quarters.

These observations are not to be regarded as a reflexion on the work recorded in this paper but as general observations because paratyphoid infections are becoming increasingly common and contamination of certain imported food-stuffs into Great Britain with *Salm. paratyphi B* has been a frequent finding in recent years.] *H. J. Bensted*

Gardner, P. S., McGregor, C. B. & Dick, K. **Association between Diarrhoea and Adenovirus Type 7.** *Brit. Med. J.* 1960, Jan. 9, 91–3, 1 chart.

There are several points of interest in this account of an outbreak of diarrhoea in young children in which adenovirus type 7 was, in a significant number of cases, isolated from HeLa cultures of the stools. The epidemiological pattern of the outbreak was complicated by the fact that the infection appeared to be mixed—*Shigella sonnei* and adenovirus, type 7, being isolated from the same specimens in a number of cases. But the picture is a little confused, as the present account is mainly concerned with the virus studies. An outbreak of diarrhoea in a town near Newcastle upon Tyne commenced at the beginning of October 1958 and between then and the end of the year there were almost 100 cases, less than half of which were bacteriologically confirmed as cases of Sonne dysentery and no other bacterial cause could be revealed. It would seem from the account given that the clinical picture was quite unlike that usually seen in a Sonne outbreak. The onset was very sudden; acute abdominal pain was followed by a watery diarrhoea, accompanied by nausea or actual vomiting, fever, headache, sore throat and cough in typical cases.

[It is not clear from the account given whether the stool specimens from which the virus was isolated (10 out of 31 examined) were the special watery type indicated above. It would be interesting to know this for it might suggest a different pathology. On the other hand most of the patients from whom adenovirus was isolated had, apart from the diarrhoea, signs and symptoms which could indicate an adenovirus infection. The state of the stool in Sonne dysentery can vary in different outbreaks and a description of the stool from patients, with a clinical picture that suggested Sonne dysentery without an added virus infection, might have been helpful. The observations recorded are very interesting but their significance must for the present remain a little uncertain.] *H. J. Bensted*

Baylet, R. J., with the technical collaboration of Mme. Khoury. Importance des shigelloses en pathologie dakaroise. [**Importance of *Shigella* Infections in Dakar**] *Bull. Soc. Path. Exot.* 1959, May–June, v. 52, No. 3, 305–17, 1 fig. [12 refs.]

This is an account of the dysenteries as they occur in Dakar and the author commences with a statement to the effect that the official monthly records of infectious diseases are quite inaccurate in respect of this group of diseases. For instance, the returns for January 1958 for Senegal showed 694 cases of amoebic dysentery as against 63 cases of bacillary dysentery [this is a fair example of the quoted figures], whereas the author's laboratory diagnosis on a representative number of stools of different types showed that in fact bacillary dysentery was 10 times more common than the amoebic form. In 219 patients with acute dysenteric symptoms passing stools containing blood and mucus shigella organisms were isolated from 77% and only 8·6% were shown to contain *Entamoeba histolytica*. All 4 *Shigella* sub-groups were well represented in a series of 667 strains isolated, but an unexpected finding was that 16% of these proved to be *Shigella dysenteriae 1* (Shiga's bacillus). Members of the Sachs-Large group were not uncommon and the Boyd organisms were found rather more frequently than might be expected. Although *Sh. sonnei* was not encountered very frequently it is of interest to note that this organism was isolated from a blood culture of an infant suffering from severe dysentery.

[This report is of interest for 2 reasons. It is remarkable that amoebic dysentery should still be diagnosed on unsupportable evidence. 20 or 30 years ago it was by no means uncommon to find workers in laboratories in the tropics identifying macrophages as entamoebae or otherwise wrongly diagnosing amoebic dysentery on a typical bacillary exudate although they were well able to recognize actively moving *E. histolytica* when confronted with a fresh preparation from a case of true amoebic dysentery. This paper should have local value in drawing attention to the backward state of laboratory diagnosis in some of the hospitals in the area covered by the author.

The other point of interest in this report concerns the frequency of true Shiga dysentery in Dakar. In most areas of the world where information is available about the distribution of the various shigella types it is quite clear that the incidence of Shiga dysentery has declined very significantly in the last 20 years. *Shigella dysenteriae 1* is now a comparatively rare isolation, even in tropical countries, where any attempt has been made to improve the general hygienic and economic position of the population. In such countries Sonne dysentery has tended to increase. This report indicates that Sonne dysentery is the least frequently seen form of bacillary dysentery seen in the area concerned.] *H. J. Bensted*

Musgrave, M. E. & Arm, H. G. **The Evaluation of Furazolidone in the Treatment of Shigellosis.** *Antibiotic Med.* New York. 1960, Jan., v. 7, No. 1, 17–21.

37 men suffering from bacillary dysentery were treated with furazolidone [this *Bulletin*, 1954, v. 29,

414; 1956, v. 31, 855], 100 mgm. 4 times a day for 7 days. All were cured clinically and 35 bacteriologically. 12 of the patients were infected with *Shigella dysenteriae*, 19 with *Sh. flexneri*, 2 with *Sh. boydii* and 4 with *Sh. sonnei*. No side-effects were noted. *A. B. Christie*

Bravo-Becherelle, M. A., Arciniega A., L., Aguilar M., Martha & Reyes, Esthela. Incidencia de diarrea en 89 lactantes de differentes estratos sociales, en relación con la presencia de *Escherichia coli* en las manos de las madres. [**Incidence of Diarrhoea in 89 Infants of Different Social Groups in Relation to the Presence of** *Escherichia coli* **in their Mothers' Hands**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1958, Dec., v. 18, Nos. 3/4, 195–202, 1 graph.

The English summary appended to the paper is as follows:—

"A group of 89 infants, whose mothers attended the Public Health Center of Tacuba (a section of Mexico, D. F.) were more or less arbitrarily divided in four groups according to the type of houses where they lived: 20 in private houses, 19 in appartments, 26 in tenements and 24 in huts, and the social characteristics of each family, the incidence of diarrhoea in each infant over 4 months, and the presence of *Escherichia coli* on the mothers' hands were studied.

"The following incidence of diarrhoea by a 12 months-old infant was found: 20 days among those living in private houses, 23 days among those in apartments, 27 days among those in tenements and 73 days among those in huts.

"*Escherichia coli* was isolated from the hands of 62 mothers and in 9 cases the strain isolated was one of the enteropathogenic group. This fact shows a large interhuman dissemination of the feces.

"The isolation of *Escherichia coli* from the mothers' hands, according to their social status, was: 15% from those living in private houses, 57.9% from those in apartments, 73.1% from those in tenements and 95.8% from those in huts.

"This shows a definite association among the social status of the families, the incidence of diarrhoea in the infants and the presence of *Escherichia coli* on the mothers' hands."

Varela, G., Kean, B. H., Barret, E. & Keegan, C. Bacteriología de las diarreas que presentan los norteamericanos en México, D.F. [**Bacteriology of Diarrhoeas among North Americans in Mexico**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1958, Dec., v. 18, Nos. 3/4, 187–90.

The English summary appended to the paper is as follows:—

"Diarrheas appear to be quite common among American tourists in Mexico.

"The authors cultured the feces of sixty two American students who came to Mexico during the summer of 1958. Twenty seven of these students suffered diarrhea and the culture of their feces gave the following results: *E. coli* (enteropathogenic) 11 cases; *Paracolobactrum*, 27 cases; *Proteus morganii*, 1 case."

Bothwell, P. W. **Brucellosis in the Oxford Regio** *Med. Officer.* 1960, Feb. 12, v. 103, No. 7, 85–9 2 diagrams & 1 fig. [55 refs.]

The author reports on some of the findings of working group on brucellosis set up in the Oxfo region. The group draws its members from medi officers of health, medical staff of the public hea laboratory, veterinary officers and staff members of agricultural research station. It is clear that there a need for a two-way flow of information. The d covery of human infections should lead to a sear for the infected cattle, as the majority of human inf tions in Britain are milk-borne. Also the occurren of infection in herds, especially (as is often the ca with tuberculin-tested milk) if the milk is n pasteurized, should be brought to the notice of cli cians in the area so that an awareness of brucello may be created. The results of a study of case reco of admissions to hospitals in the Oxford area over t 20 years (1939–1958) are analysed. 61 patients we diagnosed as suffering from brucellosis during t period. There has been no significant reduction in t number of cases diagnosed in recent years in spite of considerable increase in the proportion of milk wh is pasteurized. This may be due to an increased awa ness of the disease but it is considered that hospi admissions represent only a fraction of the true in dence as the less severely affected are treated general practitioners. As the disease is not notifia its true incidence is difficult to determine. A surv is being carried out to determine the presence of agg tinins in the sera of blood donors and in expect mothers attending antenatal clinics. A follow- examination of human placental tissues and an exa nation of tonsillar tissue removed at operation is a being made. The results of these investigations awaited.

The use of vaccination with the S.19 strain *Brucella abortus* has done much to reduce the incide of infection in herds. It is recommended that t should be limited to calf vaccination as the reappe ance of agglutinins in an adult cow can then be tak as presumptive evidence of infection. The pres legislation as to the institution of pasteurization ord and the disposal of infected cattle provides no adequ control over the disease. It is suggested that a pi scheme to attempt to creat a brucella-free zone in Oxfordshire area would be a commendable project.

[The risk of acquiring a wearisome attack of bruc losis and of it remaining undiagnosed still persists Britain and unpasteurized TT milk should be regarc as potentially suspect.] *Frederick J. Wrigh*

Goret, P., Grollet, L., Pilet, C. & Dumonteil, Sur l'évolution des anticorps brucelliques chez étudiants de l'Ecole Vétérinaire d'Alfort. [**Devel ment of** *Brucella* **Antibodies in Students at t Veterinary School at Alfort**] *Bull. Acad. N Méd.* 1960, v. 144, Nos. 1/2, 36–42.

The authors report on the presence of se agglutinins for *Brucella* found among veterin

students at Alfort in June 1958 and January 1959. The course of instruction lasts 4 years and students from each of the 4 years submitted sera. After the end of 3 years students may act as locum tenens during the holidays for veterinary practitioners but before this students may also have the opportunity to assist at calving and in removing retained placentae from cattle. As there is much less call for such assistance to be given to ewes and as in the area of France from which the students were drawn the infection is predominantly bovine, it can be assumed that positive serology indicates a reaction to infection by *Br. abortus*. The presence of seroreactors during the first year indicates that some students have taken an active interest in cattle before starting on the veterinary course and also suggests that some infections may be acquired from dust by inhalation or through the conjunctiva. The percentage of students in each of the 4 years found to have been infected rose steadily from 14 to 16% in the first year to 52 to 88% in the fourth years. Of these students only a few showed clinical signs and there was little correlation between the titres in which antibodies were detected and evidence of clinical disease but there was evidence of the titres in individuals gradually increasing, suggesting that occult infections produced increased resistance to the disease during the period of training.

Tests were also carried out for agglutination with *Rickettsia burneti*. Only one positive reaction was found, confirming that there was no cross-agglutination between the antibodies produced in brucellosis and Q fever. *Frederick J. Wright*

SALAMANDRA, R. Sull'andamento della brucellosi e delle infezioni tifo-paratifiche nel Comune di Grosseto negli ultimi 10 anni. [**The Course of Brucellosis and of Enteric in the Last 10 Years in the Commune of Grosseto**] *Riv. Italiana d'Igiene*. 1959, July–Aug., v. 19, Nos. 7/8, 249–63, 6 figs. [17 refs.] English summary (8 lines).

Grosseto is a town in Tuscany with a 1957 population of 46,500 and the author describes the progress of these 2 infections from 1948–1957.

He points out that this region has always had a high incidence of brucellosis and over the 10-year period 97 cases were notified with peaks in 1953 and 1956 of 18 and 19 cases respectively; 74 were in males, 58 were in the age-groups 21–50 and 50% were in agricultural workers. There was a definite seasonal incidence from April till June with a peak in May.

For the enteric group the total number of cases notified in the decennium was 114; 53 of these occurred in 1948 and 1949, 34 of which were in females. The incidence gradually fell till only 3 cases occurred in 1957. There was a definite seasonal incidence with peaks in August and November and a high level in July, September and October. The age-groups mostly affected were the 6–15 and 21–40 especially the 21–30 group and the author states that the decline has been more marked in females [this is not evident from tables 8 and 9]. He concludes (1) for brucellosis, the incidence is high and is not tending to fall; (2) for the enteric group the position is reasonably satisfactory and he considers that infection is mainly by inter-human contact. [For enteric there is practically no suggestion of infection by eating contaminated raw foodstuffs which plays so large a part in maintaining these infections elsewhere. In table 10 the total figure for the 60 + age groups should be 3 and not 5.]
W. K. Dunscombe

GANADO, W. & BANNISTER, W. **Bacteraemia in Human Brucellosis.** *Brit. Med. J.* 1960, Feb. 27, 601–3. [10 refs.]

The authors report on a study of 93 cases of brucellosis observed in St. Luke's Hospital, Malta. The diagnosis was supported by serum agglutination of *Brucella melitensis* to a titre of at least 1:160 and *Br. melitensis* was cultured from 74 cases (69·8%). Bone marrow cultures from 45 of these yielded *Br. melitensis* in 30 (66·7%). Simultaneous culture of blood and marrow from 35 cases showed a similar result in 21 (16 both positive, 5 both negative). In 7 cases the marrow culture was positive and the blood culture negative but also in 7 cases the reverse held true, *i.e.* the marrow culture was negative while the blood culture was positive. A careful statistical analysis showed no relation between the presence or height of fever and the presence or absence of demonstrable bacteriaemia. The occasional occurrence of persistent bacteriaemia in patients remaining afebrile was confirmed. All these observations were carried out on patients before they were given antibiotics.

It is concluded that although the blood may be re-infected from the marrow other foci of persistent infection may account for recurrent bacteriaemia. The lack of correlation between fever and bacteriaemia lends support to the view that pyrogens from bacterial or cellular breakdown may be responsible for fever [this *Bulletin*, 1958, v. 33, 869]. It is suggested that the significance of leucopenia and bacteriaemia without fever in brucellosis provide a useful field for research into the mechanism of production of fever in man.

[This is a well conducted valuable study.]
Frederick J. Wright

BURNS, G. C. T., ESPINER, E. A. & PERRY, E. G. **"Cat Bite" Disease. Report of a Case.** *New Zealand Med. J.* 1959, Oct., v. 58, No. 327, 598–9, 2 figs. on pl.

In infection following cat bite *Pasteurella septica* (*multocida*) is sometimes isolated. The disease is a localized pyogenic reaction going on slowly to abscess formation. Osteomyelitis is common, the sharp fangs carrying the infection beneath the periosteum or directly into the joint.

The authors describe a case in which a pure culture of *P. septica* was obtained from pus in the bitten hand; a metacarpo-phalangeal joint was involved and had to be curetted. Chloramphenicol and penicillin had been given but healing was achieved only after the joint had been filled with penicillin powder at the time

of curettage. It is probably necessary to maintain high blood levels of penicillin for at least 5 days when signs of infection develop after cat bites.

Charles Wilcocks

DEPAILLAT, A., LACOSTE, J. & LOMBARD, H. Charbon humain et épizootie complexe (bovins, porcins, vison et chien). [**Human Anthrax and an Epizootic in Various Animal Types**] *Bull. Acad. Nat. Méd.* 1960, v. 144, Nos. 3/4, 56–8.

The main purpose of this account of a chain of cases of anthrax in man and animals in the Department of Corrèze was to draw attention to the continuing danger of anthrax infection and also to stress that official regulations do not appear to include the carnivores among animals that may suffer the infection.

On October 25, 1957, a cow severely ill with fever and dyspnoea was killed by bleeding in its stall. Microscopic examination of the blood revealed many immobile rod forms. Another cow in the same cowshed suffered similar but less severe symptoms but recovered in several days by treatment with penicillin.

Some liver from the dead cow was then consumed at a mink farm where after 2 or 3 days 160 animals died of anthrax. In the meantime a dog which had drunk blood of the first cow died of septicaemia with high fever and dyspnoea. A sow at the farm suffered a similar fate.

The farmer developed a typical anthrax lesion on the right forearm with some fever but recovered rapidly after early treatment with large doses of penicillin. A man engaged in work at the abattoir where the first cow had been cut up became gravely ill with a very severe cutaneous lesion and systemic involvement from which he recovered but with persisting evidence of a complicating glomerulo-nephritis.

As anthrax was not, in the eyes of the law, regarded as an infection transmissible to carnivores, the 160 mink were skinned and the pelts were disposed of for commercial use.

There is a short discussion of the points raised by this history of an outbreak of anthrax which involved human, bovine, porcine, carnivorous and canine animals.

M. E. Delafield

LEVIN, S. E. & REEF, I. **Tetanus Neonatorum. A Review of 53 Cases.** *Med. Proc.* Johannesburg. 1960, Jan. 16, v. 6, No. 1, 3–7. [13 refs.]

Of 53 cases of tetanus neonatorum in the Baragwanath Hospital, Durban, 28 were treated with intragastric feeding and sedation by phenobarbitone 1 grain every 8 hours supplemented by paraldehyde 1 cc. intramuscularly every 2–6 hours; the other 25 were treated by intravenous infusion with chlorpromazine 2·0–6·0 mgm., promezathine 1–2·5 mgm., and pethidine 1·5–5·0 mgm. all per lb. body weight per day, supplemented when necessary by paraldehyde 1 cc. every 8–12 hours. The second regime made for easier management of the patient and better control of the spasm but did not reduce mortality. At least some of the deaths in the second group were not directly due to tetanus but to electrolyte and other disturbances and the authors feel that with more skilful control of intravenous method results would compare favourably with the intragastric method of sedation and with treatment by muscle relaxants and tracheotomy.

A. B. Christie

WRIGHT, R. **Tetanus Neonatorum.** *South African Med. J.* 1960, Fev. 6, v. 34, No. 6, 111–13. [22 refs.]

This is a review of 217 cases of tetanus neonatorum treated in the King Edward VIII Hospital, Durban. Various combinations of phenobarbitone, chloral hydrate and chlorpromazine were used as sedatives but results showed that there was little to choose between them. Tracheotomy was performed on 17 patients, all of whom died. The mortality from the whole group was 82·5%. Tribal customs of applying foreign material to the umbilical cord are probably the main cause of the high incidence of tetanus neonatorum. A campaign against the customs, active immunization of pregnant women, and possibly the administration of tetanus antitoxin prophylactically to all new-born babies in endemic areas are suggested as means of reducing the high incidence and mortality. [See also this *Bulletin*, 1956, v. 31, 148.] *A. B. Christie*

RINDGE, Mila E. **Tetanus Experience in Connecticut, 1950–1959.** *Connecticut Health Bull.* 1960, Feb., v. 74, No. 2, 35–40, 1 fig.

The reported incidence of tetanus in Connecticut has diminished greatly in the past 40 years. In the quinquennium 1920–24 there were 105 cases with 82 deaths —a case mortality of 78·1%; in 1925–29 there were 66 cases all of which were fatal and in 1955–59 the number of cases was 18 with 6 deaths.

The experience of 1940–49—86 cases and 39 deaths —was described in a paper by RINDGE (*Connecticut Health Bull.*, 1950, v. 64, 184) and that of 1950–59—49 cases with 17 deaths—is here analysed and compared.

Tables set out the statistics of incidence for those 2 10-year periods by age, sex and by size of town. The case fatalities by age-groups are also compared. The age distribution of cases has changed and tetanus has become more a disease of adults than of children. The sex distribution was the same in the 2 periods and tetanus remains primarily a disease of the male. There has been a tendency for a shift in the incidence from the less populated to the more heavily populated areas although the disease has remained somewhat more prominent in rural areas. Case fatality was reduced in the under 50 age-group from 30·3% to 20·7% and in the 50 and over age-group from 80·0% to 55·0%.

Some details are given of 47 of the 49 persons who developed tetanus during 1950–59 in regard to the nature of prior injury if any, where the injury occurred and the immunization status. In some cases no history of injury was obtained and in many of the

patients the injury was so slight that no physician was seen at the time. In only 3 out of all the 47 patients was a history of previous immunization against tetanus obtained. *M. E. Delafield*

CASTILLO, C. E. & SALOM GIL, R. Tétanos neonatorum en Venezuela. Su tratamiento en el Hospital de Niños de Maracaibo. Estudio preliminar. [**Tetanus Neonatorum in Venezuela. On the Treatment in the Maracaibo Children's Hospital. Preliminary Study**] *Rev. Sanidad y Asistencia Social.* Caracas. 1959, Jan.–Apr., v. 24, Nos. 1/2, 173–201, 2 graphs. [Numerous refs.]

The authors review the history, epidemiology and incidence of the disease in Venezuela. In the Maracaibo Children's Hospital, mortality for tetanus neonatorum from 1952 to 1958 was 82·7% compared with a mortality of 36·3% for tetanus in patients over 12 years of age. In 1958 the mortality for tetanus neonatorum fell to 66% as compared with the mortality at older ages of 14·3%. The authors believe that tetanus antitoxin in a dose of not less than 60,000 units should be given intravenously to babies suffering from tetanus neonatorum. They regard thiopental sodium along with chloral hydrate, both given rectally, as the best method of sedation. *A. B. Christie*

ALHADY, S. M. A., BOWLER, D. P., REID, H. A. & SCOTT, L. T. **Total Paralysis Regime in Severe Tetanus.** *Brit. Med. J.* 1960, Feb. 20, 540–45, 4 figs. [10 refs.]

This is a record of 10 cases of severe tetanus in Malaya treated by curarization, tracheotomy and positive pressure ventilation: ages ranged from 2 to 44 years. In spite of a high standard of technique and supervision, only 2 of 10 patients survived. The common feature in all the fatal cases was the development of hypotension. The authors feel that this hypotension was due, not to the positive pressure ventilation or to sedation, but to direct action of tetanus toxin on the myocardium. Whenever an electrocardiogram was taken during hypotension it was abnormal and there was some autopsy evidence that tetanus toxin can damage the myocardium. The authors feel that the total paralysis regime saves some severely ill patients who fail to respond to sedation but that others die of tetanus toxaemia, which the regime does nothing to counteract. *A. B. Christie*

CRANDELL, D. L. & WHITCHER, C. E. **Control of Neuromuscular Manifestations of Severe Systemic Tetanus.** *J. Amer. Med. Ass.* 1960, Jan. 2, v. 172, No. 1, 15–19, 2 figs. [10 refs.]

The authors have developed a system of combined drug therapy for the treatment of severe tetanus: this consists of secobarbital 1 mgm. per kgm. every 4–6 hours intravenously for psychic sedation, methocarbamol 15 mgm. per kgm. intravenously as a first dose followed by graduated doses in continuous intravenous drip to secure muscle relaxation, and chlorpromazine 0·5 mgm. per kgm. every 8 hours intravenously to potentiate the other 2 drugs. Tracheotomy with positive pressure ventilation is usually required. The muscle relaxing effect is judged by electromyography and ventilation by ventilation meter and infra-red carbon dioxide analyser. No information is given regarding results of the method in practice. *A. B. Christie*

EDSALL, G. **Specific Prophylaxis of Tetanus. [Report to the Council on Drugs** (KAUTZ, H. D., Secretary).] *J. Amer. Med. Ass.* 1959, Sept. 26, v. 171, No. 4, 417–27.

This report is in the nature of a review of the current state of knowledge of the subject. Active and passive immunization is first dealt with and is followed by very full consideration of the use and the assessment of the effectiveness of tetanus toxoid in routine immunization procedures against tetanus. The various prophylactic reagents, methods of use and the antibody response to primary immunization and also booster doses are next considered.

The management of patients, with tetanus-prone injuries, who have been actively immunized is discussed separately from the management of a similar class of patient who has not been immunized. The prevention of tetanus after an injury is dependent on adequate surgical treatment of the injury, the extent and site of the tissue damage and the immunization history.

Under certain conditions combined active and passive immunization may be advisable, even when the patient has previously been protected with tetanus toxoid, but generally a booster dose of toxoid as soon as possible after an injury will afford an immunized person adequate protection against the development of tetanus.

Unimmunized subjects should receive prophylactic antitoxin without delay after an injury. Active immunization may be commenced at the same time but it is likely to be effective at this stage only if the dose of antitoxin is relatively small and if an extra dose of toxoid is included in the primary immunization programme.

The recommendations contained in this report are in general agreement with the views held in Great Britain regarding the specific prophylaxis of tetanus. *H. J. Bensted*

TASMAN, A. L'immunité antitétanique. [**Immunity to Tetanus**] *Ann. Inst. Pasteur.* 1959, Dec., v. 97, No. 6, 835–47, 2 figs. [13 refs.]

While not offering anything significantly new about immunity in tetanus the author's results obtained with experimental animals are in complete accord with those of other workers. Recovery from tetanus does not result in the development of antibodies which will protect the subject against a subsequent infection and the only means of affording such protection lies in

active immunization with a suitable tetanus toxoid preparation. In a group of patients whose recovery from tetanus varied from 1 to 12 months, the first injection of toxoid resulted in a primary response, as in the controls, and not a secondary response which would be expected if the original attack had led to the development of any immunity. These results were confirmed by the author's experiments with guineapigs where he showed that animals that recovered from experimental tetanus were not protected against re-infection unless they were actively immunized.

H. J. Bensted

PLESKO, I., BAKOSS, P., KMETY, E. & VACHOLD, J. Nosičstvo leptospír u ježov na Slovensku. [**Carriage of Leptospires in Hedgehogs in Slovakia**] *Českosl'ov. Epidemiol., Mikrobiol., Imunol.* Prague. 1960, v. 9, No. 1, 12–15, 1 map. [14 refs.]

The English summary appended to the paper is as follows:—

"96 hedgehogs [Erinaceus europaeus roumanicus] of various regions of Slovakia were examined for leptospirae. 34 hedgehogs gave a positive agglutination-lysis reaction with the serotype L. bratislava, serogroup australis. In 8 hedgehogs, antibodies against L. sejrö and, in isolated cases, also against L. pomona, sorex-jalna [Javanica group] and icterohaemorrhagiae were found. Strains of leptospirae from 17 hedgehogs [17·7%] were cultivated, namely L. bratislava 14 times, and once L. sejrö, L. pomona and L. sorex-jalna.

"In accordance with the findings in Poland and in Soviet Union, the hedgehog [Erinaceus europaeus roumanicus] is considered as the main carrier of L. bratislava."

GUY, Y., HOUANG, L. & PLACIDI, L. Les leptospiroses. Infections communes à l'homme et aux animaux. Bilan actuel des recherches au Maroc. Note d'épidémiologie. [**Leptospirosis. Infections Common to Man and Animals. Results of Studies in Morocco**] *Maroc Méd.* 1960, Jan., v. 39, No. 416, 29–40. [Numerous refs.]

EMANUEL, Marie L. **Investigation—Leptospiral Infections in Papua.** Reprinted from *Papua & New Guinea Med. J.* Port Moresby. 1959, Dec., v. 3, No. 3, 76–80. [11 refs.]

"Of 104 human sera from the Popondetta area, 59 (57 per cent.) contained antibodies to a titre of 1:100 or more to 12 serotypes or serogroups, with the *australis A* serogroup occurring most frequently.

"Thirteen out of 154 dogs, seven out of 20 pigs and two out of five goats showed titres of 1:100 or more to a variety of serotypes. The significance of antibodies in the domestic animals is uncertain.

"No evidence of leptospirosis was found in 61 rats and five marsupial bandicoots."

BERNARD, L. A. & SUTTON, W. C. **Infection due to Chromobacteria. Report of a Case of Pneumonia due to *Chromobacterium prodigiosum* Successfully treated with Kanamycin.** *Arch. Intern. Med.* 1960, Feb., v. 105, No. 2, 311–15, 2 figs.

VIRUS INFECTIONS

The order in this section is:—*General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Enteric group; Reovirus group; Arthropod-borne group; Others.*

AGNEW, R. A. L. **A Case of Post-Vaccinal Encephalomyelitis.** *J. Roy. Nav. Med. Serv.* 1959, v. 45, No. 4, 239–43. [11 refs.]

A naval recruit aged 15 years, unvaccinated, was vaccinated at one insertion, by the multiple pressure technique, on the left upper arm on 7th May 1959. 2 days later he complained of malaise and slight headache. On the following day the headache was severe, occipital and accompanied by photophobia. The temperature rose on the next day: headache, now frontal, photophobia and transient diplopia were present: speech was slurred and the patient drowsy: the vaccination was taking. After this the temperature fell and the patient's condition improved, but on 12th May the temperature rose again and there was a recurrence of the clinical features of the previous day; but in this second episode left sixth nerve paresis was obvious. Lumbar puncture quickly relieved symptoms: cerebrospinal fluid was normal. [The significance of the ocular palsy has to be considered in relation to the information that "a visual defect in the left eye had been noted on entry into the Navy" and that subsequently "a left internal rectus recession was performed . . . for residual left sixth cranial nerve paresis".]

There were no further episodes of encephalopathy. [The diagnosis was a presumptive one, made in spite of the short incubation period and the normal cerebrospinal fluid.] *J. Pickford Marsden*

WALLACE, D. S. **Persistent Pre-Eruptive Facial Paralysis associated with Chickenpox.** *Canadian Med. Ass. J.* 1960, Jan. 23, v. 82, No. 4, 198–9. [11 refs.]

The salient features of this case were the occurrence of right facial paralysis, in a child aged 4 years, which commenced about 1 week before the appearance of a chicken pox rash and which was still present to a considerable extent 5 months later. The only other abnormal neurological findings were transient deviation of the tongue to the right and slight weakness of the left leg with diminished knee jerk and questionable plantar response on that side.

The author attributes the symptoms to an encephalomyelitis involving the motor nucleus of the facial nerve and, to a lesser extent, that of the hypoglossal nerve and the anterior nerve cells of the lumbar cord.

The cerebrospinal fluid was not examined.

J. Pickford Marsden

TAYLOR-ROBINSON, D. & DOWNIE, A. W. **Chickenpox and Herpes Zoster. I. Complement Fixation Studies.** *Brit. J. Exper. Path.* 1959, Aug., v. 40, No. 4, 398–409, 2 figs. [13 refs.]

An investigation has been made of the antigenic relationship between zoster and varicella by determinations of the titres of complement-fixing antibodies in the sera of persons suffering from these diseases. 66 sera from 35 persons suffering from zoster and 81 sera from 25 patients with varicella were investigated. With zoster vesicle fluid as antigen zoster convalescent sera usually gave higher titres than varicella sera, and the antibody response apparently occurred earlier in zoster than in varicella. Similar results were obtained when varicella vesicle fluid and the supernatant fluids of infected amnion cell cultures were used as antigens. No antigenic difference could therefore be detected between the 2 viruses. No complement-fixing antibody could be found in the sera of 40 persons who had had varicella 5–50 years previously. In ultracentrifugation experiments carried out on zoster vesicle fluid it was found that the complement-fixing antigen was not associated with the virus particle. *D. J. Bauer*

BIRD, T. & GARDNER, P. S. **Disseminated Herpes Simplex in the Newborn.** *Brit. Med. J.* 1959, Nov. 14, 993–6, 1 text fig. & 3 figs. on pl. [13 refs.]

A 21-day-old infant became ill with a considerably distended abdomen and died within a few hours. The clinical diagnosis was cirrhosis. At postmortem examination the liver was found to be enlarged, with scattered yellow foci of necrosis. The cortex of both adrenals also contained numerous areas of necrosis. No lesions were visible in sections of nervous and other tissues examined. There was no ulceration of mouth, nasopharynx or of the rest of the alimentary tract. An agent causing HeLa cells to degenerate was isolated from a suspension of liver, but not from heart or lung, and when inoculated onto the chick chorioallantoic membrane, it produced pocks characteristic of herpes simplex. It was completely neutralized by herpes antiserum, and was not affected by antisera against a number of enteroviruses.

This case of disseminated visceral herpes without eczema is reported because of some unusual features. The infant was not premature and did not become obviously ill until the end of the third week. The only superficial lesion was a small blister on the back, not noticed by the mother, and there were no severe skin or oropharyngeal lesions. Poorly developed intranuclear inclusions were found in the liver only, and after searching through many sections. The diagnosis could only be established by the isolation of the virus. Although the liver changes were more striking, it is thought that infection of the adrenal cortex may have caused collapse and sudden death, as suggested by BRAIN *et al.* [this *Bulletin*, 1957, v. 32, 726]

The source of infection is not known. The mother had no history of infection, but no blood could be obtained from her to test for neutralizing antibody.

Janice Taverne

GRAYSTON, J. T., WANG, San-Pin. & JOHNSTON, P. B. **Asian Influenza in Taiwan—1958.** *J. Infect. Dis.* 1960, Jan.–Feb., v. 106, No. 1, 37–44, 1 fig. [15 refs.]

"One of the few epidemics of Asian influenza occurring in 1958 is reported from Taiwan. Sixteen viruses were isolated and additional cases were confirmed serologically. These cases occurred both in foreigners and in the native population. The majority of the cases studied were staff members and patients of the United States Naval Medical Research Unit No. 2 located in Taipei. There was an attack rate of 18% in the Chinese members of the staff. The epidemic reached its height during the last two weeks in November. Proven cases occurred as early as the last week in September and as late as the first week in January, 1959. Attempts to define carriers in this population by virus isolation were unsuccessful. A neutralization test for Asian influenza in monkey kidney tissue culture using hemadsorption was employed along with conventional serologic tests. Results of this test in paired serums from cases paralleled the HI and CF tests. Other findings suggested that antibodies measurable in the tissue culture neutralization test persisted longer than HI antibodies. Asian influenza strains isolated in 1958 and 1959 were found to be antigenically similar to the 1957 strains."

HOLÝ, J. Der Virusantikörpergehalt bei Frühgeborenen und normalen Neugeborenen. [**The Virus Antibody Level in Premature and Normal Infants**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 1, 1–15. [21 refs.]

Between 1956 and 1958 an investigation was made of the content of influenza and mumps inhibiting antibody in the sera of 69 premature and 114 full term infants and their mothers, who mostly lived in the Prague area. The results are presented in detail in a series of tables, which show that in premature infants the antibody titres were often lower than in full-term infants and tended to fall more rapidly after birth.

D. J. Bauer

DREIZIN, R. S., PASHKEVICH, G. A., PAKTORIS, E. A., KOROLKOVA, O. I. & KNYAZEVA, L. D. **The Etiology of Membranous Conjunctivitis.** *Acta Virologica.* Prague. 1959, Oct., v. 3, No. 4, 193–200, 1 fig. [16 refs.]

Adenovirus type 3 was isolated from 15 of 22 children with membranous conjunctivitis. Rises in

complement-fixing and virus neutralizing antibodies were detected in 15 patients from whom adequate serum pairs were available.

The main symptoms observed were pyrexia, upper respiratory catarrh and membranous conjunctivitis.

H. G. Pereira

YANG, Yen-Fei, KO, Liang-Shi, JOHNSTON, P. B. & GRAYSTON, J. T. **[Epidemic Keratoconjunctivitis (E.K.C.). Part III. Adenovirus Isolation from E.K.C.]** *J. Formosan Med. Ass.* 1959, July 28, v. 58, No. 7, 437–50, 2 figs. [27 refs.] [In Chinese.] English summary.

The English summary appended to the paper is as follows:—

"It has been shown that type 8 adenovirus can be isolated from the eyes of a large percent of patients with the clinical syndrome of epidemic keratoconjunctivitis in Taiwan. However, in some patients with a similar clinical picture, other adenoviruses have been isolated, particularly type 4, but also types 2, 3, 7 and 10. In three EKC patients from whom type 8 viruses were isolated a second adenovirus type was also isolated from the eye. Adenovirus type 8 was isolated from the throat specimens of eight patients, demonstrating for the first time that this type can parasitize areas other than the eye. The significance of the isolation of adenoviruses other than type 8 and the isolation of more than one type from patients clinically diagnosed as EKC is not clear and requires further study."

SOHIER, R., CHARDONNET, Y. & FREYDIER, J. La réaction de fixation du complément au cours et au décours des infections à adénovirus. **[The Complement-Fixation Reaction in the Course of the Disease and during Convalescence in Adenovirus Infections]** *Ann. Inst. Pasteur.* 1960, Feb., v. 98, No. 2, 204–10, 1 fig.

The diagnostic value of complement-fixation in adenovirus infections was investigated by testing 180 sera collected from 70 patients at varying times after onset of clinical symptoms. It is concluded that when a single serum sample is available, a titre of 1/64 or higher may be accepted as evidence of recent infection whereas lower titres have only presumptive value. The authors stress the diagnostic value of consecutive tests for the detection of antibody rises. Adenovirus antibody was shown to persist at relatively high levels for at least 1 year after infection. *H. G. Pereira*

KALWIJ, A. S., DEKKING, F. & RUYS, A. C. **Spread of Polioviruses in the Families of Patients.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 3, 329–35. [10 refs.]

The family contacts of 104 cases of poliomyelitis (89 paralytic) were studied. 74 of the cases were confirmed by poliovirus isolation from their faeces or those of their contacts. Poliovirus (all 3 types were represented) spread freely to family contacts especially to those under 15 years of age. The virus was more rarely isolated from adults but serological evidence suggested that mothers were more often infected than fathers. Although poliovirus infections were more prevalent in the summer than in the winter there was no seasonal variation in the spread to family contacts. The presence of type 2 antibodies might protect against type 1 poliomyelitis. Thus of 23 type 1 cases (aged 0–9) 2 had type 2 antibodies in the acute stage but of 39 healthy contacts of the same age excreting type 1 virus, 12 had type 2 antibodies. The study was divided into 2 parts, a year prior to December 1st 1957 and a year after. During the second year killed polio-vaccine had been used on a wide scale. In this year there were only 28 cases (against 266 for the 2 years) and poliovirus was isolated from 17 cases or their contacts. Of 11 contacts, 0–4 years, only 2 excreted polioviruses. Other enteroviruses were isolated from some of the cases of "poliomyelitis" or from their contacts, but the aetiological role of these viruses is not known. The role of vaccination in the low incidence of poliovirus in 1958 as opposed to 1957 is similarly not known. *A. J. Beale*

KALWIJ, A. S. & RUYS, A. C. **Some Epidemiological Aspects of Poliomyelitis in the Netherlands** *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 3, 336–42, 1 fig. [10 refs.]

An interesting statistical study of poliomyelitis in the Netherlands is presented. Before 1951, cases of paralytic and non-paralytic disease were not separately reported. The disease has been more prevalent in the rural eastern and northern provinces than in the cities in the west. The disease has shown a steady shift of incidence towards the older age-groups. This is not apparent when examining the percentage of cases at various ages but is from age-specific-attack rates. Males suffer more frequently from poliomyelitis in almost every epidemic, but in 5 out of 9 epidemics since 1929 female morbidity exceeded male for the 20–24 year age-group. This reversal of incidence is ascribed to the greater susceptibility in pregnancy and greater opportunities of infection of mothers of young children. This high incidence in young adult females was less pronounced in the Netherlands than in other countries. The incidence of the disease amongst young males who were service recruits exceeded that of their colleagues of the same age not in the services. The cohort of individuals born after the epidemic in 1929–30 paid a higher tribute to the disease in 1947, 1952 and 1956 than individuals just younger or older.

A. J. Beale

ROGER, F. & ROGER, A. État du diagnostic des infections poliomyélitiques par la réaction cinétique de séro-neutralisation pendant le mois de septembre 1959. **[The Diagnosis of Polio Infections by means of the Kinetic Seroneutralization Reaction during September 1959]** *Ann. Inst. Pasteur.* 1960, Feb., v. 98, No. 2, 224–8.

A rapid qualitative technique for measuring neutralizing antibodies to poliovirus has been described by

Lépine and the authors previously [this *Bulletin*, 1960, v. 35, 93]. A quantitative variant has been evaluated as a diagnostic procedure. Acute and convalescent sera were obtained from 71 patients and in 36 of these a positive serological diagnosis could be made owing either to the absence of antibodies or to a 4-fold increase in antibody level between the 2 specimens.

A. J. Beale

Lépine, P. Études antigéniques sur le vaccin antipoliomyélitique français. [**Antigenic Studies on French Antipoliomyelitis Vaccine**] *Ann. Inst. Pasteur.* 1959, Dec., v. 97, No. 6, 780–93, 1 fig. [24 refs.]

Lépine starts his paper by saying that there is no satisfactory method of measuring the resistance of the central nervous system to poliovirus. The best that can be done is to measure serum neutralizing antibodies. He believes a titre of 1/10 of neutralizing antibodies based on experiments in monkeys is a protective level. The rate of acquisition of poliovirus antibodies under natural conditions in France is presented as a background to the results achieved with polivaccine reported by Martin *et al.* [see below] and amplified by Lépine [see this *Bulletin*, 1959, v. 34, 954]. The value of the booster dose is reiterated. Poliovaccine has been found to be stable for at least 1 year at 4°C., but it is destroyed at higher temperatures quite quickly, for example there is a 30% loss after 25 days at 28°C. An acid *p*H was found to destroy antigen very rapidly. The particular strain of virus used is very important. The type 1 strain was selected because of superior antigenicity and now better strains of type 2 and 3 have also been selected. The question of combined antigens and immunization schedules for young infants is discussed. The following scheme is proposed. BCG vaccination at birth; 3rd, 4th and 5th months, diphtheria and pertussis as a combined antigen; 6th month, vaccination (smallpox); 7th, 8th and 9th months, poliovaccine combined with tetanus prophylactic. A booster dose of poliovaccine combined with tetanus and diphtheria prophylactics should be given, followed later by polio vaccine and tetanus prophylactic to provide good immunity against these two diseases for adults.

A. J. Beale

Martin, R., Roger, F., Damas, J. P. & Roger, A. Deux ans et demi de vaccination antipoliomyélitique (vaccin Lépine) à l'hôpital de l'Institut Pasteur. Résultats immunologiques. Importance de l'injection de rappel. [**Immunological Results after 2½ Years of Vaccination with Poliomyelitis Vaccine at the Institut Pasteur. Importance of Booster Dose**] *Ann. Inst. Pasteur.* 1959, Dec., v. 97, No. 6, 757–79, 4 figs.

This long, detailed and interesting paper gives the results of 2½ years' experience with killed poliovaccine (Lépine type) in France. This differs from conventional Salk-type vaccine in the strains of poliovirus used, the method of inactivation (combined formalin and β propiolactone at 4°C.), filtration and testing.

The results in triple-negative children were not especially good after the primary course; thus of 275 persons (triple-negative) without antibodies to any type of poliovirus before vaccination, only 12% had antibodies to all 3 types after 3 primary doses of vaccine. 64% and 88% respectively of those having antibodies to 1 or to 2 types had antibodies to all 3 types after vaccination. The response of triple-negative 1, 2 or 3 years old was worse (3%) than in children 10, 11 or 12 years old (22%). A booster or recall dose of vaccine greatly improved the results. 108 triple-negative persons were studied after the primary and booster doses. After the primary course 11% became triple-positive and after the booster dose 90%. The titres of 102 subjects who responded to the complete course of vaccine are presented. The outstanding feature, to those used to the relatively poor response to the type 1 component, is that titres to this type are higher than those to types 2 or 3.

The authors conclude that a booster dose is essential for vaccination against poliomyelitis and that with this booster the Lépine vaccine is very potent immunologically.

A. J. Beale

De Lavergne, E., Gerbaut, P., Lorrain, J., Polje, F., Gilgenkrantz, Le Moyne, M. T. & Mathieu, J. Étude des anticorps poliomyélitiques en Lorraine, avant, pendant et après vaccination par le vaccin Lépine, chez un groupe de subjets régulièrement suivis. [**Study of Antibodies to Poliomyelitis before during and after Vaccination with the Lépine Vaccine in Lorraine**] *Ann. Inst. Pasteur.* 1959, Dec., v. 97, No. 6, 848–54.

The results obtained in Lorraine with French poliovaccine are presented. These are very similar to those described by Martin *et al.* [see above]. Before vaccination 26% of the subjects were triple-positive, after the primary course 71% and after a booster dose 88%. The response to the type 1 component of the vaccine appeared to be best. In these studies there were very few (9) who were triple-negative so that an exacting test of the poliovaccine performance was not made. However, its immunizing effectiveness under field conditions was demonstrated.

A. J. Beale

Barnett, E. V. & Baron, S. **Antibody Response to Increased Amounts of Poliomyelitis Vaccine.** *Amer. J. Hyg.* 1960, Jan., v. 71, No. 1, 59–68, 6 figs. [19 refs.]

Baron *et al.* [this *Bulletin*, 1959, v. 34, 991] have previously shown that one 10 ml. dose of poliovaccine into triple-negative children resulted in a very much higher conversion rate than one 1 ml. dose. In this study they used 2 batches of vaccine, nos. 90 and 12, which were of higher than average potency in the monkey test in respect of the type 1 component and found that 10 out of 12 children showed a type 1 response. In the present study a batch of vaccine, no. 44, was chosen which had a low type 1 potency in the monkey test, in fact it contained the minimal

acceptable potency. 133 children were bled before vaccination and then given 1 dose of 1 ml., 3 ml. or 10 ml. of vaccine and bled again 2 weeks later. There were 61 triple-negative children, 19 of whom had 10 ml. of vaccine; 22, 3 ml. and 20, 1 ml. With a 6-hour inactivation period at 37°C. instead of the usual 1 hour at room temperature favoured in the United States, it was found that 47%, 27% and 15% of the children responded with a titre of 1/4 or greater to type 1 virus with 10, 3 or 1 ml. dose. The figures for type 2 were 100, 100 and 80, and for type 3, 68, 41 and 25. The response to type 1 or 2 was enhanced in children who had type 3 antibodies. Thus, 70% of those having a 10 ml. dose responded to type 1 virus among the group having prior type 3 antibodies. There were rather too few children with type 1 or type 2 antibodies to assess the heterologous effect of these antibodies. The effect of homologous antibodies was to produce a booster effect and this effect was much more pronounced with the larger vaccine doses. Thus, for children with pre-existing type 1 antibody there was a 40-fold increase among the children receiving a 10 ml. dose and only a 3-fold increase in titre in those receiving a 1 ml. dose. Similar but less striking differences were seen for types 2 and 3. No untoward effects were noted from giving the 10 ml. dose to these children.

Finally, full data of the potency tests done on batches 44, 90 and 12 in monkeys and chicks and by means of the antibody combining power test are given and compared with their potency in triple-negative children. In general, the potency in children and in control tests are in agreement, thus, vaccine no. 44 gave poorer results than the better vaccines 12 and 90. It is stated that there is evidence that the potency of recently released vaccine batches is tending to increase. It is also stated that if the potencies continue to increase to the levels obtained in 1954 and 1955 [this *Bulletin*, 1957, v. 27, 833] then the need for increased amounts of antigen in a single 1 ml. dose may be met. In the meanwhile it is suggested that a 10 ml. dose may well prove of value for rapid immunization in the face of an emergency.

This is a most valuable paper presenting as it does a comparison of control potency tests in animals and effectiveness in man. *A. J. Beale*

Sohier, R., Chardonnet, Y. & Freydier, J. Étude comparée des méthodes de recherche des anticorps neutralisants par la technique habituelle et par celle d'immuno-inactivation de Gard avant et après injection de vaccin poliomyélitique inactivé. [**Comparative Study of the Demonstration of Neutralizing Antibodies by means of the Usual Technique and by Gard's Immuno-Inactivation Technique before and after Injection of an Inactivated Anti-Poliomyelitis Vaccine**] *Ann. Inst. Pasteur.* 1960, Jan., v. 98, No. 1, 7–17, 1 fig.

A comparison of the conventional method of performing neutralizing antibody titrations and the immuno-inactivation method devised by Gard [this *Bulletin*, 1958, v. 33, 288] is presented. Sera from 38 persons were examined before and after 3 doses of killed poliovaccine for antibodies to type 2 poliovirus. 19 of these persons had antibodies detectable by immuno-inactivation before vaccination but none of them had antibodies in a conventional test with 100 TCD50 of type 2 poliovirus. After vaccination 20 still had no detectable antibodies by the conventional method but 15 of these had antibodies detectable by immuno-inactivation. The increased sensitivity of the immuno-inactivation technique was also illustrated by the detection of type 2 antibodies in a higher proportion of persons with type 1 or 3 antibodies or both than the usual method. *A. J. Beale*

Lackman, D., Gerloff, R. & Philip, R. **A Comparison of Complement Fixation and Metabolism Inhibition as Methods of evaluating Poliomyelitis Antibody Response.** *Amer. J. Pub. Health.* 1959, Dec., v. 49, No. 12, 1640–45. [13 refs.]

A comparison of complement-fixing and neutralizing antibodies (determined by the metabolic inhibition method [this *Bulletin*, 1955, v. 30, 184]) was made in 3 groups of individuals. (1) sera obtained before and after an outbreak of poliomyelitis due to type 3 in Alaska in 1954; (2) children in Montana before vaccination with Salk type poliovaccine and following the effect of successive doses of vaccine up to 4; (3) children in Idaho vaccinated in 1956 and followed for the effect of 3 doses. It was found that only in the group of children involved in the outbreak on St. Paul island in Alaska was there any evidence of an increase in the complement-fixing antibodies. Many children responded not only to type 3 virus but also to the other types in the complement-fixation test. This work confirms that of others [see, for example, Melnick *et al.*, this *Bulletin*, 1955, v. 30, 662] that complement-fixing antibodies are an indication of a relatively recent infection with living poliovirus. Thus, 8 months after the epidemic the level of complement-fixing antibodies had fallen to insignificant levels. None of the various groups of children given Salk vaccine responded with the production of complement-fixing antibodies. It was shown that the proportion of children having neutralizing antibodies to the 3 types of poliovirus increased with increasing numbers of doses of poliovaccine. However, in general, the response of the children given vaccine in 1954 and 1955 was greater than in those given vaccine in 1956. The authors think that this was in some measure at least due to the fact that the proportion of children without antibodies before vaccination was higher in 1956 than in 1954 but it could also be explained by a decline in the antigenic potency of the vaccines used in 1956 compared with those used in 1954.

A. J. Beale

Koprowski, H. **Historical Aspects of the Development of Live Virus Vaccines in Poliomyelitis.** *Trans. & Studies of College of Physicians of Philadelphia.* 1960, Jan., v. 27, No. 3, 95–106. [56 refs.]

In this lecture delivered on receiving the Alvarenga Prize Dr. Koprowski describes the pioneer role that

he and his colleagues have played in the development of attenuated poliovaccine. It is a long and discursive and often amusing lecture with full reference to the original work by himself and his colleagues. There is no consideration of critical or divergent opinions although passing mention is made of myths surrounding the origin of attenuated poliovaccine and scientists who refuse to recognize merit in others. The first child to be given oral poliovaccine received the TN attenuated type 2 strain of poliovirus on February 27th 1950 and by January 1951 20 children had been infected without ill effect and the cloak of secrecy was removed. Thereafter 2 adults were vaccinated. Koprowski strongly advocates the use of living vaccine, administering type 1 first to newborns so that active immunity is acquired under cover of maternal antibodies. The other 2 types can be given later.

There are 3 main advantages of this procedure:—

1. Antibodies are assured from the cradle to the grave (since the duration of immunity is thought likely to be lifelong).

2. Virus spread from young infants occurs very infrequently.

3. Interference by other enteroviruses is likely to be of little importance in the newborn. *A. J. Beale*

Saslaw, S., Wooley, C. F. & Anderson, G. R. **Aseptic Meningitis Syndrome. Report of Eleven Cases with Cerebrospinal Fluid Isolation of Enteroviruses.** *Arch. Intern. Med.* 1960, Jan., v. 105, No. 1, 69–75. [27 refs.]

"Virus isolates were obtained from the spinal fluid of 11 patients with aseptic meningitis. ECHO virus, type 9, was recovered from five patients, Coxsackie A, type 9, from three, and Coxsackie B, types 4 and 5, from one and two patients, respectively."

Ginevri, A.; Felici, A.; Gregorig, B. **Contribution to the Study of Diseases in Italy caused by Coxsackie B Group of Viruses. I. Clinical and Virological Aspects of an Outbreak of Bornholm Disease** [Ginevri & Felici]. *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 3, 310–16. English summary (6 lines). **II. Epidemiological, Clinical and Virological Data obtained in the Course of a Summer Outbreak caused by Coxsackie B4 Virus** [Felici & Gregorig]. *Ibid.*, 317–28, 5 figs. & 4 maps. English summary (4 lines).

I. A small outbreak of Bornholm disease in the Teramo province of Italy in the summer of 1957 is described. Until virus studies established the disease as due to Coxsackie B2 it had been thought that the Asian strain influenza virus was responsible. The presence of coughing and bronchial râles, rubella-like rash and intestinal symptoms is stressed. Coxsackie B2 was isolated from 66% of the patients. Throat swabs were a better source of virus than faeces and isolations were rare after 7 days. The viruses isolated seemed identical with each other and with the prototype strains. The viruses were isolated in monkey kidney cells but could also be propagated in KB, monkey heart and to a lesser extent in HeLa and PF line of human kidney cells.

II. The epidemiological features of an outbreak of Bornholm disease and minor illness (fever with or without headache and constipation) occurring in Gorizia in Italy during May and June 1958 is described. The illness was due to Coxsackie B4. The disease was much more frequent in children aged 7 months to 10 years and was most prevalent of all in those 4–6 years old. Bornholm disease was about equally prevalent in children 0–5, 6–10 and over 10 but minor illness was much more frequent in young children. Abacterial meningitis was present in 3% of the patients. The disease was probably spread in the main by young children, and the prevalence of sore throat and the presence of virus in throat swabs suggested that virus spread from the upper respiratory tract was of paramount importance in the epidemiology. The incubation period was usually 3–4 days but could probably be as short as 24 hours. *A. J. Beale*

Sanford, J. P. & Sulkin, S. E. **The Clinical Spectrum of ECHO-Virus Infection.** *New England J. of Med.* 1959, Nov. 26, v. 261, No. 22, 1113–22. [90 refs.]

The ECHO viruses as a group give rise to a characteristic type of illness, which in general conforms to that of the enteroviruses as a whole, though there may be individual variations in severity.

The broad differentiation of the group of enteroviruses, based on their varied action on tissue cultures and in experimental animals, is summarized in a table reproduced below.

Virus	No. of Types	Cytopathogenicity in Tissue Culture		Pathogenicity for Animals	
		HeLa Cells	Monkey Kidney	Suckling Mice	Monkeys
Polio	3	+	+	0	+
Coxsackie A	19	11, 13, 15, 18* only	9 only	+	7, 14 only
B	5	1, 3, 5 only	1–5	+	0
ECHO	24	0	+	9 only	0

+ = Virtually all strains of agent either cytopathogenic or pathogenic
0 = „ „ „ „ „ neither „ nor „
* Numbers refer to specific types usually either cytopathogenic or pathogenic.

Coxsackie viruses were originally differentiated from polioviruses by their pathogenicity for infant mice, and the 2 main groups of the former by the type of lesion which they produce in these animals. While Coxsackie A virus gives rise to inflammation of striated muscle in suckling mice and hamsters, Coxsackie B causes inflammatory lesions in the pancreas, brain and dorsal fat pad. These distinctions, however, are not quite clear cut, for recent work has shown that 2 types of Coxsackie A virus, numbers 7 and 14, are capable of producing poliomyelitis-like lesions in monkeys, and in the case of type 14 in mice also. The ECHO viruses are almost totally non-pathogenic to mice with the exception of a single variant of type 9, which causes paralysis on intra-cerebral injection in this animal.

Immunologically there is considerable blending between the main groups of enteroviruses, and the specificity of neutralization and complement-fixation tests is impaired by the sharing of common antigens between several members of each group.

The history of the discovery of the ECHO viruses explains their otherwise irrelevant name. In 1951, Robbins and his colleagues [this *Bulletin*, 1952, v. 27, 291] working in the U.S.A., isolated 2 new viruses from the stools of patients suffering from non-paralytic poliomyelitis. These agents destroyed tissue culture cells but were non-pathogenic to suckling mice and were thus described as Enteric Cytopathogenic Human Orphan viruses—orphans since they had no (then recognized) parent disease. Numerous other ECHO serotypes have since been recognized and their association with mild paralytic disease, acute aseptic meningitis and influenza-like illnesses has been demonstrated. The authors have now reviewed the clinical features of disease due to the viruses of this group, which appear to have a ubiquitous distribution.

Infection appears to cause symptoms in some 85% of cases and affects principally children and young adults. After an incubation period of 5–10 days (extreme range 2–20 days) a biphasic illness begins, the initial phase of which is characterized by fever, anorexia, vomiting and mild pharyngitis. A more protracted and severe range of symptoms begins after a brief afebrile intermission, and usually perists for 5–12 days, rarely for 3 weeks. Fever is invariable and often high; rigors not infrequently occur. Headache, nausea and vomiting are extremely common, the last especially so in children. Constipation, abdominal discomfort and colic are also frequent. Myalgia troubles about 40% of patients.

A rash develops very commonly in children and is constant in those under 3 years old. Developing early in the disease, it breaks out as a rubelliform pink or mauve, macular eruption on the face, spreading to the trunk within 8 hours. The palms and soles may be involved. ECHO virus type 6 is exceptional in not producing an exanthem; so is Coxsackie A type 9 in that it *does*. A petechial eruption is occasionally seen.

A minor degree of lymphadenopathy, mainly cervical, is found in about 20% of patients but splenomegaly may be found in as many as one-third.

The leucocyte count is not helpful in diagnosis, being often normal, sometimes moderately raised with a relative increase in the granular series while sometimes a lymphopoenia is noted. The cerebrospinal fluid, however, is abnormal in at least a third of those affected, showing a polymorphonuclear pleocytosis of up to 1,000 cells for cmm. with a corresponding rise in protein content of 40–100 mgm. per cmm. Unlike those infected with polio virus, the causal virus can be isolated from the cerebrospinal fluid in 30–50% of patients.

The virus affects the brain and cord in a small minority of patients, who may show evidence of a generalized mild encephalitis, ocular paresis, nystagmus and deafness, in fact involvement of any cranial nerve is possible. A myelopathy of motor type, or transient involvement of anterior horn cells resembling poliomyelitis may occasionally ensue.

The wide range of tissue adaptation of this group of viruses is shown by the occurrence in rare cases of myocardial, hepatic and renal damage though serious and permanent lesions do not seem to occur.

Although convalescence is often protracted permanent sequellae do not result from ECHO virus infections and no mortality is reported in this paper.

In infancy epidemic diarrhoea has been reported as due to type 18 ECHO virus, while many other strains have also been implicated. Infantile croup may be another manifestation, while Boston exanthem disease, distinguishable from rubella only by the absence of posterior cervical adenopathy, has been shown to result from ECHO type 16 virus infection. Orchitis and pleurodynia have also been reported.

[The extraordinarily wide range of manifestations of infections with viruses of the ECHO group seems to preclude clinical diagnosis. Virological investigation of the stools is clearly indicated in any epidemic or family febrile illness associated with any of the symptoms and signs recorded above.]

J. H. Walters

Eckert, G. L., Barron, A. L. & Karzon, D. T. **Aseptic Meningitis due to ECHO Virus Type 18.** *J. Dis. Children.* Chicago. 1960, Jan., v. 99, No. 1, 1–3.

"ECHO virus Type 18 was recovered from the cerebrospinal fluid and stool of a 12-year-old child with aseptic meningitis. Development of specific neutralizing antibody was demonstrated. ECHO 18 virus, previously only associated with the production of mild infantile diarrhoea, now supplements the ECHO serotypes capable of producing aseptic meningitis."

Milojcic, B. Über die Epidemiologie der Hepatitis epidemica in Jugoslawien. [**The Epidemiology of Infectious Hepatitis in Yugoslavia**] *Arch. f. Hyg. u. Bakt.* 1960, Feb., v. 144, No. 1, 7–11.

Before World War II no epidemics of infectious hepatitis were observed in Yugoslavia. At the end of the war and in the post-war years epidemics of the disease occurred in the age-group 17–25 years. Since 1950 an increasing number of sporadic cases were observed and between 1952 and 1954, outbreaks of the disease occurred in children's institutions. In

the autumn of 1955 an epidemic wave set in which reached its peak in December and disappeared by April 1956. A second but much milder epidemic occurred in the winter of 1956–7. Between 1952 and 1957 epidemics had occurred in 60% of all the children's institutions in the Belgrade area.

Analysis of the statistical data showed that the morbidity rate was higher in kindergartens than in institutions for younger children up to 2 years of age. In schools epidemics occurred only exceptionally although the number of sporadic cases was large. The incidence of the disease was usually higher in school children from the country than in the children from the city. Investigation of families showed that in those in which there were infected children, the disease did not usually spread to other members, at any rate not in icteric form.

Information obtained by questionnaire about 1,149 children of all ages who suffered from hepatitis showed that the most vulnerable age group was 7–14 years.

Biochemical liver function tests indicated that for each icteric case there were between 2 and 3 of atypical infection. The results of these tests and of clinical examination carried out in a follow-up during 3 years of a group of children who had had typical and atypical infections demonstrated the persistence of liver damage in 60% of the icteric cases.

In 3 institutions the prophylactic value of injections of gamma globulin was examined but no significant result was obtained. *M. E. Delafield*

GEORGIADES, J. & ZAREMBA, Wanda. **Comparative Investigations of the Behaviour of the Aldolase Test, Urobilinogenuria Test and the Colloid Oscillation Test on the Blood Serum of Persons from the Environment of Patients affected with Hepatitis epidemics.** *Bull. Inst. Marine Med. Gdańsk.* 1959, v. 10 Nos. 1/2 59–63.

65 people living together with patients suffering from epidemic hepatitis were examined for evidence of this disease. 33 of them showed a considerably increased level of the enzyme aldolase and urobilinogen in their urine. 17 showed only the increased enzyme level, but the urine was normal, and in 15 no abnormality could be discovered. When these people were examined clinically, and when serum lability tests for changes in the serum proteins were applied, no correlation could be discovered between the rise in aldolase and positive results with the lability tests. This is thought to be due to the fact that the aldolase may become changed in the early stages of the acute disorder, whereas alterations in serum proteins appear as a consequence of rather than together with damage to the liver. *H. Lehmann*

SIEDE, W. & KLAMP, A. Die Behandlung der akuten Virus-Hepatitis mit Corticoid-Derivaten. **The Treatment of Acute Viral Hepatitis with Prednisone or Prednisolone**] *Deut. med. Woch.* 1960, Feb. 26, v. 85, No. 9, 333–41, 369–70, 8 figs. [47 refs.]

In a previous publication [this *Bulletin*, 1957, v. 32, 408] the authors of this paper reported on the definite value of prednisone in the treatment of acute viral hepatitis. Other workers have confirmed this finding in general although their opinions have varied somewhat about the indications for and effects of this therapy.

In the present paper there is a detailed account of experience of 140 cases of viral hepatitis with prednisone and prednisolone, in which this treatment had a favourable effect, confirmed statistically, in bringing about a rapid diminution in the serum bilirubin level, improving the patient's condition and lessening the duration of jaundice. The indications and contra-indications of this therapy are considered at considerable length, with description of the side-effects which occurred in some patients. The dosage was usually between 40–60 mgm. each day for 5 days but continued for longer periods when clinically indicated, and later the dose was reduced gradually. When the total dosage had been high or therapy had continued for more than 3 weeks corticotrophin was administered. Except in certain cases prednisolone showed no advantage over prednisone. Stress is laid on the importance of additional supportive treatment by bed rest, careful diet, administration of vitamin B complex and amino-acid mixture. Antibiotic treatment is suggested in cases in which dosage with prednisone or prednisolone has been high or of long duration.

M. E. Delafield

HADDOW, A. J. **Studies on the Biting Habits and Medical Importance of East African Mosquitos in the Genus** *Aëdes.* **I. Subgenera** *Aëdimorphus, Banksinella* **and** *Dunnius. Bull. Entom. Res.* 1960, Jan., v. 50, Pt. 4, 759–79, 5 figs. [Numerous refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1960, v. 57, 653.]

AMERICAN J. TROP. MED. & HYG. 1959, Nov., v. 8, No. 6, 644–722, numerous figs. [Numerous refs.] **Ecologic Studies of Japanese Encephalitis Virus in Japan.**

I. *Introduction.* (W. F. SCHERER and E. L. BUESCHER, pp. 644–50.)

Japanese encephalitis (JE) was studied in Japan first because it is an important disease there and secondly, because it is in an area where no other group B arborvirus occurs and this resolves many of the difficulties which exist in the interpretation of serological results elsewhere. The geography of the study areas in the Kanto Plain is reviewed, notably the areas surrounding two large heronries at Sagiyama and Shinhama.

II. *Mosquito infection.* (E. L. BUESCHER, W. F. SCHERER, M. Z. ROSENBERG, I. GRESSER, J. L. HARDY and H. R. BULLOCK, pp. 651–64.)

Mosquitoes were trapped at the heronries and in other areas by a variety of methods including traps baited with various wild birds (notably herons), chickens, cattle, pigs and man. Only species attracted in large numbers to bird-, pig- or human-baited traps

or to cows or chickens were tested for virus by inoculation of mice. *Culex tritaeniorhynchus* and *C. pipiens* were virtually the only species in bird-baited traps. *Anopheles sinensis* was numerous only in pig-baited traps. 298 of 300 strains of JE were isolated from *C. tritaeniorhynchus* and 2 from *C. pipiens*. None were isolated from over 16,000 *A. sinensis*. Isolations were made from late June until early October, but in 1956 infections were detected several weeks earlier at Sagiyama than at Shinhama. The maximum population of *C. tritaeniorhynchus* in heron-baited traps was in July and the maximum number of isolations was made shortly afterwards as the mosquito population was declining. Maximum infection rates in mosquitoes therefore correspond in time with human and equine epidemics. The estimated population of *C. tritaeniorhynchus* around the heronries was over 10^6. Taking a positive pool of mosquitoes to contain only 1 infected mosquito, infection rates varying from 2 to 50% were found. The infection rate increased steadily during the summer, remained high in September, then declined. Infection rates varied in the same place from year to year without, apparently, being correlated to total mosquito population. Large numbers of *C. tritaeniorhynchus* and *C. pipiens* collected from April to June in 1953 and 1957 failed to yield virus. The virus may pass the winter in hibernating female mosquitoes, but these are very few in number.

III. *Mosquito factors. Zootropism and vertical flight of C. tritaeniorhynchus with observations on variations in collections from animal-baited traps in different habitats.* (W. F. Scherer, E. L. Buescher, M. B. Flemings, A. Noguchi and J. Scanlon, pp. 665–77.)

7 different species of wild bird were compared for attractiveness to *C. tritaeniorhynchus* by using bait traps. Different numbers of birds of different sizes were used so as to give approximately the same body area in each trap. Common birds of species with high and low incidences of JE antibody were compared. Traps with black crowned night herons (BCNH—*Nycticorax nycticorax*) attracted significantly more *C. tritaeniorhynchus* than 6 other species. Chicken-baited traps attracted as many *C. pipiens* as BCNH or more. *C. tritaeniorhynchus* was less common than *C. pipiens* with all other birds than BCNH and little egrets (LE—*Egretta gargetta*). Pig-baited traps attracted more *C. tritaeniorhynchus* than BCNH which in turn attracted more than man; *C. pipiens* was attracted almost equally to the 3; *A. sinensis* was attracted mainly to pigs. *C. tritaeniorhynchus* frequently fed on the animals in the traps and pigs and birds became infected with JE in this way. At Sagiyama infections of BCNH had been detected in nests as much as 60 feet above ground. Bird-baited traps were therefore set at 24 and 50 feet above ground: *C. tritaeniorhynchus* was consistently taken in small numbers in these traps and 9 of 11 BCNH in these traps developed JE antibody during August/September. Some traps were inherently more effective in mosquito catching than apparently identical traps in comparable positions. The reasons for these differences were not elucidated, but differences in microhabitat may be important. Traps from which the bait had been removed continued to attract mosquitoes in decreasing numbers for at least 3 days. The host-preference of *C. tritaeniorhynchus* was not affected by proximity to large populations of a single host species (*e.g.* herons). The species is mainly rural in distribution.

IV. *Avian infection.* (E. L. Buescher, W. F. Scherer, H. E. McClure, J. T. Moyer, M. Z. Rosenberg, M. Yoshii and Y. Okada, pp. 678–88.)

Nestling and flightless juvenile birds were mainly studied because they could be captured. Their ages were estimated by measurement to ± 1–3 days. Approximately 5% of the total bird population in the study sites or up to 10% of nestlings in the heronries were examined each year. Maternal haemagglutinin-inhibiting (HI) antibody persists less than 15 days, so HI antibody in older birds indicated past infection. In the 2 heronries 68 strains of JE were isolated from birds, 54 from free-living birds and 14 from sentinel BCNH in mosquito traps. Of the 54 free living birds, 35 were BCNH, 16 plumed egrets (PE—*Egretta intermedia*) and 3 LE. Suckling mice did not seem to be more sensitive isolation hosts than weaned mice. Virus isolations were confined to August and early September. Infections were also timed as 7 days before HI antibody was first detected in sentinel birds being bled weekly. In this way, infections were detected throughout August and the first half of September. 48 of 82 sentinal BCNH developed HI antibody and viraemia was detected in 11. The HI test was 10 times more effective than virus isolation in detecting infection in free-living birds.

Infection frequencies rose from 0–5% in early August to 31–44% in early September; 2 weeks later infection rates were nil. In 2 heronries 150 miles away similar timing of infections was found—at one of these, nestling cormorant (*Phalacrocorax carbo*) infections were also demonstrated in July/August. Blue magpies (*Cyanopica cyaneus*) had previously been shown to have a high (49%) incidence of JE antibody [this *Bulletin*, 1958, v. 33, 443], but infections were not detected in young birds in this study. The higher incidence of infection in BCNH than in PE or LE pre-presumably reflects the biting preference of *C. tritaeniorhynchus* for the former.

Estimates of adult populations in the heronries from aerial photographs were 2,400–3,600 and 3,000–5,400 at the peak in July, and as 22% of 18 BCNH, 77% of 18 PE and 15% of 12 LE were without antibody there may be thousands of susceptible adults in these colonies. There were estimated to be between 300 and 2,000 susceptible nestling and juvenile birds in one heronry by mid-July when infections began. The time sequence of the infection curve in birds fitted that of the curve of mosquito infections.

V. *Avian factors.* (W. F. Scherer, E. L. Buescher and H. E. McClure, pp. 689–97.)

BCNH, LE and PE seem to be equally susceptible to JE infection; the effect of age on susceptibility is not clear. The effects of maternal antibody were discussed in a previous paper [this *Bulletin*, 1960, v. 35, 483].

When BCNH with antibody following natural infections were challenged subcutaneously with $10^{7.7}$ mouse LD50, viraemia did not occur even though the birds were treated with cortisone. Similarly, PE with antibody inoculated intravenously with 10^9 LD50 had no viraemia. Nestling herons and egrets have soft downy skin for the first 2–3 weeks which exposes them to heavy attack from mosquitoes: after 3–4 weeks feathers cover them except on the legs and near the eyes, providing some protection. Two nematodes are described which frequently attach to the oesophagus and stomach of young birds and which might conceivably be alternative vectors of JE, although there is no evidence of this.

Great egrets (*Egretta alba*) and cattle egrets (*Bubulcus ibis*) breed in May, June and early July and nestlings are no longer present when JE infection is present in the mosquitoes. Adult herons and egrets fly as far as 20 miles from the colonies daily in search of food and they may thus be a source of circulating virus for mosquitoes over a wide area. They migrate south, mainly from August onwards and start to return in April. There is no evidence that birds bring virus to Japan with them on their northern migration from tropical and temperate Asia—probably however, some birds are still circulating virus on at least the early part of their southern migration.

VI. *Swine infection.* (W. F. Scherer, J. T. Moyer, T. Izumi, I. Gresser and J. McCown, 698–706.)

Studies were made of 10–20% of the 500–1,000 pigs near one of the heronries and of pigs in mosquito traps. In May 68 of 80 (85%) young farm pigs had maternal antibody, but only 34% had antibody in early August. Between late July and early September, 97 of 98 farm pigs developed HI antibody. Studies on the pigs in traps showed that infections started in late July, and that infections of pigs also occurred in Tokyo, but 2–3 weeks later than in 2 rural areas. Viraemia was detected in several trap pigs. No infections occurred in samples of 51–124 pigs in April–June. As an estimate of pig populations it was found that 57,000–72,000 pigs were born annually in a single prefecture of 1,500 square miles near Tokyo. Apart from breeding sows, pigs live through 1 JE season only, being slaughtered at 10–16 months of age. Most pigs are born either in February–April or in September–November. More pigs are slaughtered annually than the combined total of cattle, horses, goats and sheep and these animals are usually 2 or more years old when slaughtered. Susceptible pigs are thus very numerous and the infections in them are closely correlated with the timing of mosquito and avian infections.

VII. *Human infection.* (W. F. Scherer, M. Kitaoka, T. Okuno and T. Ogata, pp. 707–15.)

About 200 children near each of the heronries were studied for serological evidence of infections between June and November. In June the incidence of antibody near Shinhama rose from 8% at 6 years of age fairly steadily to 46% at 12 years; near Sagiyama 27% of children aged 6–8 years had antibody. By October–November 14 of 295 children without previous antibody had developed HI antibody, while 7 of 109 with neutralizing antibody in June showed a 4-fold or greater increase in HI antibody. At Sagiyama all antibody responses occurred between mid-August and mid-September; at Shinhama they extended to late October. Viraemia was not detected in these children, none of whom had recognizable symptoms of infection. Outbreaks of encephalitis occur annually in Tokyo and there is a tendency for large outbreaks with a peak in early or mid-August to alternate in successive years with smaller outbreaks which have their peak in September. From the timing of a limited number of patients with encephalitis diagnosed in the laboratory as JE, these epidemics are believed to be mainly or entirely attributable to this virus. For every clinical case of encephalitis there must be many inapparent and mild infections. For instance, in the areas surrounding the children studied in this paper, about 67,000 children live in one and 28,500 in the other. The results suggest infection rates of 5%, implying that 3,350 and 1,400 children would be infected in each in a single epidemic season.

VIII. *Survey for infection of wild rodents.* (W. F. Scherer, E. L. Buescher, C. M. Southam, M. B. Flemings and A. Noguchi, pp. 716–8.)

95 rodent sera (species unknown) collected in 1953–4 had no JE neutralizing antibody. In June–July 1954 none of 87 *Rattus norvegicus* and of 11 *R. rattus* had HI antibody; in November (after the JE season) none of 118 *R. norvegicus* and of 54 *R. rattus* had antibody. Experimentally *R. norvegicus* develops HI antibody in response to infection, as do mice. Of 163 rodents of various species collected in 1956–7 only 1 *Apodemus speciosus* had HI, but not neutralizing antibody. A further *A. speciosus* had neutralizing but not HI antibody. It is highly improbable that rodents of the species examined are significantly involved in maintenance of JE in Japan.

IX. *Epidemiologic correlations and conclusions.* (E. L. Buescher and W. F. Scherer, 719–22.)

The annual cycle of JE in Japan can be divided into the pre-emergence period (April–June), the virus dissemination period (July–September) and declination to eclipse thereafter. Virus can be detected first in the vector, *C. tritaeniorhynchus*, 2–3 weeks before pig or avian infections become detectable. Pig and avian infections become common when the total vector population has already begun to decline. Once virus appears in mosquitoes it is rapidly transferred and multiplied in the amplifier hosts—birds (mainly BCNH) and pigs. Man is much less frequently attacked by *C. tritaeniorhynchus* than pigs or birds and is, therefore, not involved until the infection rate in the vectors is high. Virus is probably spread over wide areas by the flight of viraemic birds. From these studies control must obviously depend on breaking the chain of infection. Removal of the pigs or birds is not feasible nor is control of the culicine mosquitoes. Only mosquito screening of houses (which are not particularly suited to this) and vaccination (and there is as yet no satisfactory vaccine) remain. [This is an important series of papers with much practical detail and well-thought discussion which must be read in full.] *C. E. Gordon Smith*

ZAKORKINA, T. N. & NAUMOV, K. L. **[The Results of a Serological Examination of Mammals and Birds in a Focus of Tick-Borne Encephalitis at the Construction Site of the Krasnoyarsk Hydro-electric Power Plant (Siberia)]** *Med. Parasit. & Parasitic Dis.* Moscow. 1959, v. 28, No. 4, 463–9. [Numerous refs.] [In Russian.] English summary.

An investigation has been made of the incidence of complement-fixing antibody to tick-borne encephalitis virus in wild birds and small mammals caught in an area affected by this disease in Krasnoyarsk, Siberia. The tests were carried out with a reference antigen on centrifuged saline extracts of the livers and spleens, which were investigated for the presence of antibody. Positive results were obtained with 21 of 104 birds belonging to 15 species, and with 41 (25·3%) of 162 small mammals belonging to 9 species. *D. J. Bauer*

ERRATUM

In the abstract of the paper by PAPP, this *Bulletin*, 1960, v. 35, 166, the word "rubella" should read "measles" throughout.

SERGIENKO, A. D. **The Use of the Chick Red Cell Haemolysis Reaction in the Diagnosis of Haemorrhagic Nephroso-Nephritis.** *Problems of Virology.* London. 1958, v. 3, Nos. 5/6, 380–84. [32 refs.] [Translated from Russian.]

To 2-fold dilutions of sera in saline an equal volume of 1% washed chick cells is added. The mixtures are incubated at 37°C. for 15 minutes after which haemolysis indicates a positive reaction. Titres of 1:20 or greater are considered positive. 89% of 85 sera from the patients suffering from haemorrhagic nephroso-nephritis were positive, about half with titres greater than 1:20. 69% of 37 sera from patients who had recovered from the disease were positive, more than half having titres over 1:20. In contrast 5 of 254 healthy persons, 2 of 52 typhus patients, 5 of 23 patients with infective hepatitis, 1 of 8 with kidney disease, 1 of 13 with skin diseases, 1 of 14 with bladder diseases and 1 of 36 with other infectious diseases were positive—all at 1:20 except 2 at 1:40. These patients were from outside the endemic area of haemorrhagic nephroso-nephritis. From the endemic area 66% of 328 apparently healthy persons and 64% of 28 persons with other diseases had positive sera. In endemic areas 78–84% of long-term residents had positive sera compared with only 45% of those who had resided there for less than a year. From a village outside the endemic area only 2% of 254 persons had positive sera. In individual patients with haemorrhagic nephroso-nephritis titres rose from 1:10–1:20 3–16 days after onset of the disease, to 1:20–1:160 7–50 days after onset. 4-fold or greater increases in titre were demonstrated in 6 of 7 patients. The titre late in the disease is apparently maintained for at least 5 years.

Sera heated at 56°C. for 30 minutes lose their haemolytic activity, but this is restored by addition of fresh guineapig serum. Sera heated at 75°C. for 20 minutes do not have their activity restored by addition of fresh guineapig serum. Fresh guineapig serum alone does not cause haemolysis. On storage of serum at 4°C. there is a progressive loss of activity which can be restored by addition of fresh guineapig serum. When sheep, rabbit, guineapig and fish erythrocytes and those of haemorrhagic nephroso-nephritis patients were used, no difference was found in haemolytic activity between the sera of normal individuals and those of haemorrhagic nephroso-nephritis patients.

C. E. Gordon Smith

DROZDOV, S. G. **The Rôle of Domestic Animals in the Epidemiology of Biphasic Milk Fever.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 4, 103–8, 1 fig. [Translated from Russian.]

Areas in a district of Moscow where biphasic milk fever had been reported annually since 1948 were studied. The highest incidence was in May–June with a few cases in September–October. Both sexes and all ages and occupations were equally affected. 90% of the cases were in family or group outbreaks, several patients becoming ill within 2–4 days. Most outbreaks were in families possessing goats or cows or both. In other incidents cases occurred on the farm and in the population supplied with milk from it. The cases were diagnosed by neutralization and complement-fixation tests.

Milk samples were collected every 5–10 days in the spring from 150 goats and cows. From 203 samples from goats 2 strains of virus were isolated by intracerebral inoculation of mice and a further 2 after 1 blind passage. They were identical with the biphasic milk fever virus. No isolations were made from cows' milk. 2 ixodiid ticks are common in the area, *Ixodes ricinus* and *Dermacentor pictus*. The seasonal incidence of infestation of domestic animals with *I. ricinus* fitted the occurrence of biphasic milk fever. 700 fasting or partially engorged female ticks in 8 pools of *D. pictus* and 4 of *I. ricinus* were inoculated into mice. A virus identical with that of biphasic milk fever was isolated from a pool of 99 *I. ricinus* collected from cows on 11 May. Ticks appear to attack human beings rarely in this area and the incidence of antibody in 46 unaffected persons was only 6·5% compared with up to 40% in areas where Russian spring-summer virus is transmitted by ticks to man. 4 of 20 goats had neutralizing antibody; 16 of 66 goats and 35 of 60 cows had complement-fixing antibody. The higher incidence in cattle may be due to their longer life-span and the lower incidence in goats may mean that more of them are susceptible to infection and thus to excreting virus in the milk.

1,200 female *I. ricinus* trapped in the focus were fed on a non-immune cow, but virus was not isolated from blood and milk tested every 1–2 days for 20 days—the animal, however, developed antibody. Another cow was inoculated daily for 8 days with 20 ml. of a 10% suspension of mouse brain infected with a human strain of virus (strain F). Virus was isolated from blood on the 2nd day and from milk on the 15th day. Cattle thus appear to excrete virus in the milk only after enormous infecting doses.

The treatment of animals with insecticides and the boiling or pasteurization of milk is suggested for prophylaxis in infected foci. *C. E. Gordon Smith*

GROSSMAN, L. A. & WOLFF, S. M. **Acute Thrombocytopenic Purpura in Infectious Mononucleosis.** *J. Amer. Med. Ass.* 1959, Dec. 19, v. 171, No. 16, 2208–10, 1 fig.

A case is reported of infectious mononucleosis in a man of 25, presenting with thrombocytopenic purpura, epistaxis, and haemoptysis as the only symptoms. The blood picture on admission showed 12·5% atypical lymphocytes and monocytes, and the heterophil agglutinin test in absorbed serum was positive in a dilution of 1:96; the platelet count was 4,000/cmm., the bleeding time 17·5 minutes and clotting time 16 minutes. There were a few palpable cervical lymph nodes, but no unusual enlargement.

Prednisone 60 mgm. daily was given for 8 days from admission, and subsequently in reduced dosage. There appeared to be an immediate response to this treatment, the platelet count rising steeply to 200,000 on the 8th day, and the bleeding time falling to 6 minutes on the 3rd day. The haemorrhagic symptoms also cleared rapidly.

At least 23 cases of infectious mononucleosis with thrombocytopenic purpura have been described since 1942. *H. Stanley Banks*

SYMMERS, W. St. C. **Generalized Cytomegalic Inclusion Body Disease associated with Pneumocystis Pneumonia in Adults. A Report of Three Cases, with Wegener's Granulomatosis, Thrombotic Purpura, and Hodgkin's Disease as Predisposing Conditions.** *J. Clin. Path.* 1960, Jan., v. 13, No. 1, 1–21, 26 figs. [42 refs.]

Cytomegalic inclusion disease may be found in 1 to 15% of necropsies on infants dying from other conditions: it is usually confined to the salivary glands and is of little clinical significance. In adults it is very rare and tends to occur as a generalized infection complicating some other condition, notably Hodgkin's disease, leukaemia, refractory anaemias and some collagen diseases. It is frequently associated with pneumonia due to *Pneumocystis carinii*. The use of steroids, antibiotics and cytotoxic drugs may predispose to cytomegalic inclusion disease. In the 3 cases described, 1 patient suffered from Wegener's granulomatosis, 1 from thrombotic purpura and 1 from Hodgkin's disease. Cytomegalic inclusion disease and pneumocystis infection were found in all 3 at necropsy. Clinical and histological details are given, there is a full discussion and the article is well illustrated.

A. B. Christie

OLÁH, P. **Studies on the Occurrence in Human Sera of Complement Fixing Antibodies to Contagious Canine Hepatitis Virus.** *Acta Microbiologica. Budapest.* 1959, v. 6, No. 2, 113–16. [12 refs.]

Complement-fixing antibody to canine hepatitis virus was found in the sera of 72 of 308 (23%) healthy persons [the titres are not stated] and also in 29 of 106 (27%) patients with infective hepatitis and in 5 of 39 (12%) with serum hepatitis. There was thus no evidence of any antigenic relationship between canine and human hepatitis. Negative results were obtained with the sera of 6 laboratory workers who had been handling the virus. *D. J. Bauer*

Bacteriology and Immunity

The order in this section is:—**General; Bacteriostatic and Bactericidal Substances; Bacteria; Rickettsiae; Bacteriophages; Viruses; Immunity.**

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-divisions of this section.*

GENERAL

COETZEE, J. N. **Methods of Analysis of Long-Term Experiments for the Determination of Mutation Rates of Bacteria.** *South African J. Lab. & Clin. Med.* 1959, Dec., v. 5, No. 4, 236–47, 4 figs. [19 refs.]

Mutation rates can be reliably estimated by prolonged observation of bacterial populations in continuous culture, so that the exponential phase of growth is maintained for a large number of generations. This method avoids the huge sampling errors

associated with short-term observations. The author expounds the mathematical theory of the dynamics of populations of 2 types of bacteria, the wild type and the mutant. Three situations are considered in some detail: (i) equal growth rates, with both forward and backward mutation; (ii) equal growth rates, with no back-mutations; (iii) unequal growth rates, with no back-mutations. *P. Armitage*

WEBB, S. J. **Factors affecting the Viability of Air-Borne Bacteria. I. Bacteria aerosolized from Distilled Water.** *Canadian J. Microbiol.* Ottawa. 1959, Dec., v. 5, No. 6, 649–69, 11 figs. [33 refs.]

For measurement of death rates in the airborne state the test bacteria were suspended in water and mixed with an appropriate amount of a suspension of killed bacteria of the same strain grown in the same fashion except that radioactive phosphorus was incorporated in the medium. By this means the effect of settling could be distinguished from death. For measurements up to 10 seconds, a continuous flow tube was connected to the atomizer; for longer studies the suspension was held in a rotating drum.

Death occurred in 2 stages, the first rapid kill being observed during the first second after formation of the cloud and being followed by a slower kill that continued over the 5 hours of the experiment. The rates of kill in the 2 stages varied independently and were influenced by relative humidity and temperature, as well as by the bacterial species. Details must be sought in the original but it is suggested that an important factor leading to death of the bacteria is the breaking of protein-water bonds with consequent breakdown of the protein structure. No intermediate humidity was found to give the highest death rate and it is suggested that when such optima have been observed by other workers, they were generally due to some constituent of the medium from which the bacteria were sprayed [see also this *Bulletin*, 1958, v. 33, 683; 1959, v. 34, 473]. *R. E. O. Williams*

KANDLER, O. & KANDLER, Gertraud. Die L-Phase der Bakterien. [**The L Phase of Bacteria**] *Ergebn. Mikrobiol. Immunitätsf.* 1960, v. 33, 97–127, 5 figs. [Numerous refs.]

BARRY, G. T., TSAI, Tien-Hu & CHEN, F. P. **Chemical and Serological Relationships of Certain Bacterial Polysaccharides containing Sialic Acid.** *Nature.* 1960, Feb. 27, v. 185, 597–8. [11 refs.]

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

The order in this section is:—**General; Antibiotics; Colicines; Other Therapeutic Substances; Disinfection.**

GOUREVITCH, A., HUNT, G. A. & LEIN, J. **Structure-Activity Relationships in a Series of Synthetic Penicillins.** *Antibiotics & Chemotherapy.* New York. 1960, Feb., v. 10, No. 2, 121–8, 3 figs.

KNOTHE, H., WAGNER, G. & WITT, G. Über Penicillin-Serumspiegel nach einmaliger Anwendung eines wässrigen Depot-Penicillins. [**Serum Penicillin Level after Single Intramuscular Injection of Depot-Penicillin in Watery Suspension**] *Deut. med. Woch.* 1959, Oct. 2, v. 84, No. 40, 1820–21, 1844, 2 figs.

This is a simple study of the rate of disappearance of penicillin from the blood after a single large dose of a depot preparation. This was Megacillin, containing per dose 200,000 units of sodium penicillin and 800,000 of 1-*p*-chlorbenzyl-2-pyrrolidylmethylbenzimidazole-penicillin (*i.e.* a compound of penicillin and an antihistamine). This was given to 25 normal adults and to 41 patients. Blood levels after 2, 3, 4 and 5 days are presented in 2 different graphic forms: 94% of subjects had a therapeutic blood level (0·03 unit/ml. or more) after 2 days and 79% after 3 days.

The interest in the paper is in the further investigation of the 4 subjects in whom the level fell abnormally rapidly. In 3 of them the same test was repeated later with the same result: in 1 a dose of procaine penicillin also vanished from the blood within 24 hours. It therefore appears that there is a small minority of people who for some reason eliminate penicillin with exceptional rapidity. [If this finding should be further verified, it will not be easy to explain, since in fact the prolonged action of a depot preparation depends on its slow absorption from the site of injection, and not on any reluctance of the kidneys to eliminate it.] *L. P. Garrod*

HOIGNÉ, R. & SCHOCH, K. Anaphylaktischer Schock und akute nicht-allergische Reaktionen nach Procain-Penicillin. [**Anaphylactic Shock and Acute Non-allergic Reactions after Procaine Penicillin**] *Schweiz. med. Woch.* 1959, Dec. 26, v. 89, No. 52, 1350–56. [63 refs.]

These authors distinguish 2 types of immediate reaction to penicillin. One is the familiar anaphylactic shock, of which they describe 6 personal cases. In 3 of these patients' sensitivity was subsequently demonstrated by a skin test: this was not only locally positive, but in each case re-produced shock (the proceedings used were intradermal injection of 10 units

in 1 case and 500 in another, and scarification through a 100,000 unit/ml. solution). A serological test for sensitivity of which no details are given was also employed in 5 cases and was positive in 3. Tests by both methods for sensitivity to procaine were always negative.

The other type of reaction, of which 16 cases are described, was of even more rapid onset and shorter duration, and consisted largely of sensory disturbances, including giddiness, tinnitus, a metallic taste, sometimes diplopia or blurred or distorted vision, paraesthesiae, anxiety and restlessness. Skin tests in 7 of these patients and serological tests in 14 showed no evidence of sensitivity to either penicillin or procaine. These symptoms are said to resemble those resulting from intravenous injection of procaine: the authors have never seen them produced except by procaine penicillin, and they say they cannot exclude the possibility that accidental intravenous injection may have caused them. *L. P. Garrod*

GILLISSEN, G. Die Beziehung zwischen Penicillin- und Streptomycinresistenz und Gehalt an Desoxyribonucleinsäure (DNS) bei *M. pyogenes* var. *aureus* und *E. coli*. [**The Relation between Penicillin and Streptomycin Resistance and Deoxyribonucleic Acid Content in** *Staphylococcus aureus* **and** *E. coli*] *Ztschr. f. Hyg. u. Infektionskr.* 1959, v. 146, No. 1, 97–104, 2 figs. [Numerous refs.]

When a sensitive staphylococcus was rendered resistant to penicillin its deoxyribonucleic acid (DNA) content (expressed as DNA in relation to total N content) increased. When *Escherichia coli* was made resistant to streptomycin the opposite change took place. The author has previously found that a brief treatment with deoxyribonuclease reduces the proportion of penicillin-resistant cells in a population of staphylococci. He now reports that such treatment increases the proportion of streptomycin-resistant cells in a population of *E. coli*. [In the multiple tests of which the results are given in a table this effect was not consistent, and many of the differences seem too small to be significant: a viable count on a population of 10^9/ml. cannot be highly exact, especially when obtained by spreading an inoculum of 0·3 ml. over 10 agar plates.] *L. P. Garrod*

HORIUCHI, T., HORIUCHI, S. & MIZUNO, D. **Non-participation in Protein Synthesis of the RNA synthesized in the Presence of Chloramphenicol in** *Escherichia coli*. *Japanese J. Med. Sci. & Biol.* 1959, June, v. 12, No. 3, 99–107, 3 figs. [40 refs.]

This paper describes experiments which are said to show that ribonuclease formed by *Escherichia coli* in the presence of chloramphenicol, this antibiotic being removed after 1–2 hours by washing the cells, does not participate in the subsequent formation of cell protein, β-galactosidase or phosphomonoesterase.
L. P. Garrod

OKAMOTO, S.; HIROKAWA, H.; ABE, M.; MIZUNO, D.; OHTAKI, K. **Mechanism of Chloramphenicol Resistance in** *E. coli*. **I. The Drug Sensitivity of Chloramphenicol-Resistant Strains of** *Escherichia coli* **as determined by the Assessment of 50% End Points** [OKAMOTO]. *Japanese J. Med. Sci. & Biol.* 1959, June, v. 12, No. 3, 109–17, 7 figs. **II. Sensitivity alteration to Various Drugs of Chloramphenicol Resistant** *E. coli* **converted to Protoplast** [HIROKAWA, ABE & MIZUNO]. *Ibid.*, 119–24, 2 figs. [10 refs.] **III. The Total Amino-Acid Composition of Chloramphenicol Resistant** *E. coli* **and Electrophoretical Pattern of its β-Galactosidase** [OKAMOTO, OHTAKI & MIZUNO]. *Ibid.*, 125–31, 2 figs. [10 refs.]

This series of papers examines some different hypotheses as to the basis of resistance to chloramphenicol.

I. The method of most of the experiments described here was to cultivate *Escherichia coli* in a medium containing different concentrations of chloramphenicol for a short (but apparently variable) period, estimate growth by turbidity measurement, and plot this against antibiotic concentration. This gave a straight line of a certain slope, which was simply displaced when the test was done with a resistant variant, suggesting, in the authors' view, that the mode of action of chloramphenicol on resistant organisms is the same as that on sensitive organisms, rather than that resistance depends on some change in metabolism. The behaviour of the resistant variant in relation to other antibiotics was also examined, and one experiment is described showing that the resistant variant does not destroy the antibiotic.

II. Sensitive and resistant *E. coli* were converted to protoplasts by glycine treatment, and (by a proceeding of which no details are given) the lethal concentrations of chloramphenicol for protoplasts and intact cells were compared. There was a small difference between these in sensitive cells and a greater one in resistant, but it is evident that "a considerable resistance still remained within the protoplast".

III. This paper examines the possibility that resistance to chloramphenicol is based on a change in metabolism, and so far as it goes reveals no such change. Comparing the sensitive and resistant variants of the same strains of *E. coli*, no significant difference was found in total amino acid composition, nor was any difference demonstrable by electrophoresis in β-galactosidases formed in the presence of lactose.
L. P. Garrod

ERLANDSON, A. L., FISHER, M. W., GAGLIARDI, Leola A. & GAETZ, Marjorie R. **The Comparative Activity of Chloramphenicol against Gram-Negative Bacilli** *in vitro* **and in Experimental Infections in Mice.** *Antibiotics & Chemotherapy.* New York. 1960, Feb., v. 10, No. 2, 84–7.

"Comparative tests were made to determine the activity of chloramphenicol in vitro and in experimental infections in mice, employing 35 strains of

commonly found gram-negative bacilli. These strains included representatives of the following genera: *Aerobacter, Escherichia, Klebsiella, Paracolobactrum, Proteus, Pseudomonas,* and *Shigella.* It was concluded that inhibition by less than 25 μg./ml. by broth dilution test and the presence of any inhibition zone around the 30 μg. disc indicated probable amenability to chloramphenicol in vivo."

BURNS, L. E., HODGMAN, Joan E. & CASS, A. B. **Fatal Circulatory Collapse in Premature Infants receiving Chloramphenicol.** *New England J. of Med.* 1959, Dec. 24, v. 261, No. 26, 1318–21, 2 figs. [21 refs.]

At the Los Angeles County Hospital it has been customary to treat premature infants born more than 24 hours after rupture of the membranes with antibiotics "because of assumed exposure to infection". Apparently because some suspicion arose that this remedy was more dangerous than the (potential) disease a comparison was made between the effects of different treatments and none. 4 groups of 32, 30, 33 and 31 premature infants were respectively given (1) no antibiotics, (2) chloramphenicol 100–160 mgm./kgm. daily, (3) procaine penicillin 150,000–600,000 units and 50 mgm./kgm. streptomycin daily, (4) all these 3 antibiotics in the same doses. All the antibiotics were given intramuscularly at 12-hour intervals. The mortality of the untreated group was 19% (causes of death in this group are not stated: it would be interesting to know how many of them did in fact develop such infections as the antibiotics are intended to prevent). In the group given penicillin and streptomycin the mortality was 18%. Chloramphenicol produced a mortality of 60% and all 3 antibiotics of 68%. These babies remained apparently well for 2 or 3 days, then developed successively vomiting, refusal to suck, respiratory distress, abdominal distension, diarrhoea, flaccidity, an ashen colour and hypothermia, with death usually on the 5th day. Chloramphenicol blood levels climbing to about 70 and 170 μgm./ml. before death were determined in 2 babies. No consistent changes were found *post mortem.*

Some reasons why the premature infant may be unable to tolerate chloramphenicol are suggested [but none is offered for supposing that it should be necessary to give a dose equivalent to as much as 10 gm. daily to an adult]. The paper concludes: "the use of prophylactic antibiotics has been discontinued in this nursery". *L. P. Garrod*

TRUSS, F. & BERGERHOF, H. D. Kanamycin und Nierenfunktion. Ein Beitrag zur Anwendung von Kanamycin in der Urologie. [**Kanamycin and Renal Function: a Contribution to the Use of Kanamycin in Urology**] *Deut. med. Woch.* 1960, Jan. 22, v. 85, No. 4, 151–5, 1 fig. [20 refs.]

This paper, also from Göttingen, deals with 21 patients, 13 of whom were submitted to prostatectomy, 5 to other operations on the urinary tract, and 3 to none, all of whom were given kanamycin, usually 1 gm. daily, sometimes 1·5 and in 1 case 2 gm., the total dose varying from 9 to 22·5 gm. 5 had normal renal function and the rest some degree of impairment: in 8 of the latter further impairment resulted from the treatment and 2 of them became deaf. A second large table gives the results of a series of renal function tests performed in 20 of the cases before and after the course of treatment. It is concluded that the use of kanamycin should be avoided if possible in patients with defective renal function, and that if it has to be given, dosage should be controlled by estimations of the antibiotic content of the blood. [The main interest of this paper is in the comparison between the results of no less than 8 tests of renal function.] *L. P. Garrod*

BAYER, W. Klinische Erfahrungen mit Kanamycin. [**Clinical Results with Kanamycin**] *Deut. med. Woch.* 1960, Jan. 22, v. 85, No. 4, 155–8, 172. [14 refs.]

This author from Ulm first presents the results of testing for sensitivity to kanamycin 1150 strains of 13 varieties of bacteria. A second table states the clinical results ("very good", "good" or "uncertain") of its employment in 6 different conditions (without bacteriological diagnoses). The numbers of very good results were bronchopneumonia 8 of 14 cases, peritonitis 11/19, septicaemia 8/10, mediastinitis 0/1, secondary osteomyelitis 4/6, infected third-degree burns 1/5. Some cases were treated by local instillation into wounds or abscess cavities. No toxic effects were seen: the dose never exceeded 0·5 gm. twice daily in adults and only 1 course exceeded 9 days in length.

L. P. Garrod

SCHATTENFROH, C. Erfahrungen mit Kanamycin in der Chirurgie. [**The Use of Kanamycin in Surgery**] *Deut. med. Woch.* 1960, Jan. 22, v. 85, No. 4, 145–50, 171–2. [11 refs.]

This paper from the Surgical Clinic of the University of Göttingen, after furnishing particulars of the sensitivity to kanamycin and other antibiotics of locally-isolated strains of some common bacteria, reports in detail the results of the use of kanamycin in 41 surgical cases. Tables give particulars of each of these, including age, bacteriological findings (in most), previous treatment, dose of kanamycin (usually 1 gm. daily) and duration of course, and results, both as to recovery and in the nature of toxic effects. The organisms found were in every case either staphylococci, *Escherichia coli, Proteus* or enterococci. There were 10 skin, wound or soft tissue infections treated for 4 to 15 days, all with good effect, 5 cases of peritonitis, 4 originating in appendicitis, 3 of which were treated locally (up to 1 gm. of solution intraperitoneally) as well as systemically with good results

in 4, 2 of haematogenous and 2 of secondary (compound fracture) osteomyelitis, all improved, and 22 of urinary infection, including 15 patients submitted to prostatectomy. The results in this last category were more variable, and include the only examples of toxic effects: 1 patient had urticaria, 6 impairment of renal function, and 2 deafness. *L. P. Garrod*

ERLANGER, B. F. & GOODE, Louise. **Antibacterial Activity of Acyclic Decapeptide Analogs of Gramicidin S.** *Science.* 1960, Mar. 4, v. 131, 669–70, 1 fig.

WATERWORTH, Pamela M. **The Antibacterial Properties of Leucomycin.** *Antibiotics & Chemotherapy.* New York. 1960, Feb., v. 10, No. 2, 101–8, 1 fig. [10 refs.]

"The antibacterial activity of leucomycin has been compared with that of four other antibiotics of the macrolide group. It differs from that of erythromycin, spiramycin, and oleandomycin but is indistinguishable from that of carbomycin. The minimum inhibitory concentrations of leucomycin and carbomycin are the same for a variety of bacteria, including staphylococci, streptococci, and species of *Clostridium*. Leucomycin and carbomycin exhibit complete cross resistance, and are affected to the same degree by changes in *p*H and by the presence of erythromycin when acting on staphylococci exhibiting the dissociated type of resistance to the latter antibiotic."

OGINSKY, E. L., GREEN, G. S., GRIFFITH, D. G. & FOWLKS, W. L. **Lethal Photosensitization of Bacteria with 8-Methoxypsoralen to Long Wave Length Ultraviolet Radiation.** *J. Bacteriology.* 1959, Dec., v. 78, No. 6, 821–33, 7 figs. [22 refs.]

It has been known for many years that methylene blue sensitizes bacteria to light. Recently it has been found that plant furocoumarins have a similar effect, and these authors have made a detailed study of the factors affecting this action in 8-methoxypsoralen. This substance is not itself lethal, and the light used had no lethal effect in 10 minutes, but irradiation of bacteria suspended in a solution of 8-methoxypsoralen caused a rapid and steep fall in the viable count: of the 2 organisms used, *Staphylococcus aureus* was the more susceptible, the count falling to *nil* in 2 minutes: 2 strains of *Escherichia coli* were killed rather less rapidly. Unlike the action of methylene blue, that of 8-methoxypsoralen is not dependent on the presence of oxygen. The bactericidal effect was found to be more rapid at low temperatures than high throughout the range 0–45°C.: this again differs from the effect of methylene blue. Other factors studied were the concentration of 8-methoxypsoralen, *p*H, the age of the culture, and the composition of the culture medium. *L. P. Garrod*

MACCALLUM, F. O. & NOBLE, W. C. **Disinfection of Anaesthetic Face Masks.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1959, Nov., v. 18, 183–4.

Small volumes of cultures of 4 pathogenic bacterial species or of tissue culture fluid containing Coxsackie virus were dried on the tubing or face mask of anaesthetic apparatus. Contact with the rubber did not kill them. Washing for 2 minutes in water at 60°C. destroyed the bacteria and "most of the virus". Heat is therefore recommended for disinfecting such apparatus. The tubing withstands boiling: this damages the mask, which should therefore be placed in water at 60–70°C. for 2 minutes and then rinsed under running water at the same temperature for a further 2 minutes. *L. P. Garrod*

BACTERIA

The order in this section is:—**Cocci; Donovania; Mycobacterium; Corynebacterium; Haemophilus; Pseudomonas; Pfeifferella; Enteric Organisms; Brucella; Pasteurella; Bacillus; Anaerobes; Spirochaetes; Erysipelothrix; Listeria; Others.**

DUVAL, M.; GERMAN, A.; LELUC, R. Recherches sur l'anti-hyaluronidase streptococcique. I. Dosage turbidimétrique de l'acide hyaluronique [DUVAL & GERMAN]. [**Studies on Streptococcal Anti-hyaluronidase. I. Turbidimetric Estimation of Hyaluronic Acid**] *Bull. Soc. Chimie Biol.* 1959, v. 41, No. 12, 1613–20, 2 figs. [13 refs.] II. Dosage de l'anti-hyaluronidase streptococcique dans le sérum [GERMAN, DUVAL & LELUC]. [**II. Estimation of Streptococcal Anti-hyaluronidase in the Serum**] *Ibid.*, 1621–8, 3 figs.

GAUSE, G. F., KOCHETKOVA, G. V. & SORBAEVA, N. A. **Rate of Appearance of Mutants with Respiration-Deficiency in Staphylococci.** [Correspondence.] *Nature.* 1959, Dec. 5, v. 184, Suppl. No. 23, 1821–2.

Incorporation of albomycin (50 units/ml.) into nutrient medium resulted in selective detection of respiratory deficient mutants of *Staph. aureus* (strain 209). In the absence of albomycin the growth of these non-acid producing mutants was inhibited by the acids

produced by the parent strain. Mutant colonies were recognized by their orange, red or rose colour. The frequency of appearance of these mutants was about 1 per 10^8 cells both in the presence and absence of highly polymerized deoxyribonucleic acid extracted from the mutant organisms. [Other interpretations of the evidence that acid production by the parent strain inhibits the growth of mutant organisms are possible.]

H. Gooder

KASĂROV, L. Über eine neue biochemische Eigenschaft der Staphylokokken. [**On a New Biochemical Quality of Staphylococci**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 3, 305–8, 2 coloured figs. on pl.

The English summary appended to the paper is as follows:—

"A new biochemical activity of staphylococci, the degradation of carotin to colourless compounds (carotinolysis) is reported.

"Out of 250 staphylococcus strains tested 126 proved carotinolytic. There was considerable parallelism between the betahemolytic and carotinolytic activity of staphylococci. Out of 126 carotinolytic strains 114 (90.4%) proved hemolytic. Out of the non-hemolytic strains 82.2 per cent did not show any carotinolytic activity."

MANDELSTAM, J. & ROGERS, H. J. **The Incorporation of Amino Acids into the Cell-Wall Mucopeptide of Staphylococci and the Effect of Antibiotics on the Process.** *Biochem. J.* 1959, Aug., v. 72, No. 4, 654–62, 3 figs. [32 refs.]

This is a study of the utilization by staphylococci of glycine and 3 other amino-acids: these were labelled with ^{14}C and estimated separately in the protein and cell wall material ("mucopeptide") after 1 hour's incubation in a medium also containing glucose and phosphate buffer, with or without penicillin and other antibiotics. The experiments described in most detail were made with glycine. In the absence of penicillin this amino-acid was incorporated almost entirely in the cell wall mucopeptide, the glycine of the protein being 2% labelled and that of the mucopeptide 41%. Chloramphenicol did not interfere with this process. The other amino-acids similarly incorporated in mucopeptide were glutamic acid, alanine and lysine. In the presence of all 4 amino-acids and penicillin, mucopeptide synthesis was slowed for 45 minutes and arrested thereafter: some evidence was obtained that the mucopeptide formed was of abnormal constitution. Bacitracin also reduced mucopeptide synthesis, and chlortetracycline prevented it completely. [The concentration of antibiotics used was high: penicillin was included at 100, 1,000 and subsequently 500 units per ml. "because in this strain of staphylococci, penicillinase formation can be induced by penicillin", and 70 μgm./ml. chloramphenicol was also included in tests with penicillin to prevent this. There is no further information about the degree of penicillin resistance of this organism, and the applicability of the findings to normal strains is not discussed.]

L. P. Garrod

HANCOCK, R. **The Amino Acid Composition of the Protein and Cell Wall of** *Staphylococcus aureus*. *Biochim. et Biophys. Acta.* 1960, Jan. 1, v. 37, No. 1, 42–6. [14 refs.]

HANCOCK, R. **Accumulation of Pool Amino Acids in** *Staphylococcus aureus* **following Inhibition of Protein Synthesis.** *Biochim. et Biophys. Acta.* 1960, Jan. 1, v. 37, No. 1, 47–55, 7 figs. [20 refs.]

ELLIOTT, W. H. **Aminoacetone Formation by** *Staphylococcus aureus*. *Biochem. J.* 1960, Mar., v. 74, No. 3, 478–85, 3 figs. [20 refs.]

NUNNERY, A. W., TINKER, Mary & BRADFORD, W. L. **Effect of Sodium Chloride Concentration on Staphylococcal Agglutination.** *Proc. Soc. Exper. Biol. & Med.* 1959, Dec., v. 102, No. 3, 707–9, 1 fig.

Suspensions of a few strains of staphylococci were tested for agglutination with homologous antisera in the presence of various concentrations of sodium chloride. The highest titre was observed with concentrations between 1·3 and 1·7%. Preliminary washing of the suspension in 0·85% salt solution abolished its agglutinability. *R. E. O. Williams*

DÓBIÁS, G., BALLÓ, T. & KEMÉNYVÁRI, J. III. Über den directen Nachweis von Staphylokokken-α-Toxin aus Eiter. Die klinische Bedeutung des Verfahrens. [**III. The Demonstration of Staphylococcus α-Toxin in Pus. The Clinical Importance of this Procedure**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, Dec., v. 118, No. 6, 459–65.

Dilutions of the supernatant fluid from centrifuged pus (*e.g.* from an empyema) were mixed with a 2% suspension of rabbit red blood cells and incubated at 37°C. That haemolysis in this system was due to staphylococcal α-toxin was suggested by the facts that haemolysis was, in almost all cases, restricted to rabbit cells; it was prevented by heating the pus dilutions to 56°C. for 1 hour and by the addition of antitoxin. There seemed to be a relation between the titre of toxin in the pus from patients with empyema and the clinical severity of their disease. It is suggested that the determination of toxin in pus can be used as a method of rapid diagnosis. *R. E. O. Williams*

STREITFELD, M. M., SALLMAN, B. & SHOELSON, S. M. **Staphylocoagulase Inhibition by Pooled Human Gamma-Globulin.** [Correspondence.] *Nature.* 1959, Nov. 21, v. 184, Suppl. No. 21, 1665–6, 1 fig. [11 refs.]

The authors investigated the effect of gamma globulin on staphylococcal coagulases in an attempt to

explain its therapeutic effect in staphylococcal infections. The addition of 27·5 mgm./ml. of gamma globulin delayed the clotting of plasma by 19 out of 24 strains of coagulase positive staphylococci for 24 hours and 5 strains for a shorter time. Clots formed by these organisms failed to dissolve after 24 hours in the presence of gamma globulin but globulin free from preservative did not inhibit bacterial growth.

Partially purified free and bound coagulase of 5 strains of *Staphylococcus aureus* were prepared and the amount of gamma globulin necessary to inhibit their actions was measured. This varied from 0·0067 to 0·013 mgm./ml. necessary to inhibit bound coagulase and from 0·11 to 0·43 mgm./ml. to inhibit free coagulase, these were smaller amounts than is present in normal human blood. There were slight variations between different preparations of gamma globulin. Experiments on the action of gamma globulin against other staphylococcal products are in progress.

M. Patricia Jevons

BÖHME, D. & BOUVIER, C. A. **Influence of Infection upon the Reticuloendothelial System, Internal Organs, and Distribution of Circulating Leucocytes of Normal Albino Mice.** *J. Infect. Dis.* 1959, Nov.–Dec., v. 105, No. 3, 222–37, 20 figs. [45 refs.]

Animals injected with bacterial endotoxins develop an enhanced immunity, even against bacteria antigenically unrelated to the endotoxins. In this paper the authors describe changes in the immune status of infected mice. One group of mice was injected intravenously with *Staphylococcus aureus*: a second group received *Mycobacterium fortuitum*, also intravenously and a third group of mice acted as uninoculated controls.

Mice injected with *Myco. fortuitum* showed splenic and hepatic enlargement, due mainly to progressive granulomatous formation, and increased capacity over normal controls in ability to phagocytose colloidal carbon.

The mice receiving *Staph. aureus* did not develop hepatic or splenic enlargement and were no better than normal controls at phagocytosing carbon particles. Since hepatic and splenic lesions in these cases were mild, the conclusion is reached that staphylococci either do not stimulate the mouse reticulo-endothelial system or that they produce a toxic inhibitor of the system.

Both types of infection caused a polymorphonuclear leucocytosis, and the mice infected with staphylococci showed haematopoietic metaplasia in their lymph nodes.

Detailed histological descriptions are provided. Both types of infection caused extensive abscess formation in the kidneys [this *Bulletin*, 1956, v. 31, 80] and fatal pyelonephritis. *Myco. fortuitum* caused a systemic disease with formation of granulation tissue and epitheloid-like cells. The absence of caseation and giant-cell formation was similar to the results of infection with *Myco. tuberculosis* in mice. *J. McKay*

STOLLERMAN, G. H., SIEGEL, A. C. & JOHNSON, Eloise E. **Evaluation of the "Long Chain Reaction" as a means for detecting Type-Specific Antibody to Group A Streptococci in Human Sera.** *J. Exper. Med.* 1959, Dec. 1, v. 110, No. 6, 887–97. [19 refs.]

Bactericidal tests were carried out on sera from patients known to have suffered from infections with Type 12 Group A streptococci [this *Bulletin*, 1958, v. 33, 173] and those which gave the strongest and weakest positive reactions were tested by the long chain test.

For this test the sera under test were mixed with broth cultures of Type 12 streptococci previously found to be suitable, and incubated for 4 hours at 37°C. without shaking. The organisms were also incubated with normal rabbit serum and rabbit serum containing T 12 M antibody. Mixtures were examined microscopically and the "long chain index" calculated by dividing the mean chain length of cultures grown in test serum by the mean chain length of cultures grown in normal rabbit serum.

The long chain index of these sera ranged from 3 to 14 (average 9); sera producing the strongest bactericidal test produced the highest long chain index. This reaction was specific and absorption of sera with cells of homologous type but not heterologous types, removed the long chain effect.

Tests on serial samples of sera from convalescent patients showed that the long chain index was 3·8 on 35th day and the bactericidal test was positive at 60 days; both were strongly positive at 170th day.

A comparison of the 2 tests on 217 acute and convalescent sera from 99 patients showed that there was close agreement and the 2 tests were almost equally sensitive. 66 were positive by the bactericidal test and 63 by the long chain test.

The authors stress that the indicator strain must be carefully selected and maintained in a virulent form but some strains rich in M antigen do not form long chains in the presence of homologous antiserum [*ibid.*, 1959, v. 34, 385]. Test sera must be free from inhibitors, contaminants and antibiotics; however, the authors believe that this test has the advantage of simplicity over the more complicated bactericidal test and mouse protection test. *M. Patricia Jevons*

CRAWFORD, Y. E. **Studies of a Complement-Fixing Antigen from Group A Streptococcal L Forms. I. Preparation and Preliminary Tests in Rabbits and Man.** *J. Immunology.* 1960, Jan., v. 84, No. 1, 86–92.

Antigen was prepared by extracting saline washed suspensions of the streptococcal L form GL 8 [this *Bulletin*, 1957, 32, 703] with physiological saline for 10 minutes at 90–94°C. This procedure is optimum for obtaining a preparation free of anticomplementary properties. Rabbit sera were obtained from animals immunized with GL 8 and also heat-killed streptococci of Groups A, B, C and D. The human sera studied were from 107 persons, classified in 7 different categories with regard to their recent experience of streptococcal and other upper respiratory infections.

The complement-fixation test showed that the L form was antigenic in the rabbit. Antibody titres to the L form developed also in rabbits immunized with streptococci of groups A and C. Other streptococcal vaccines failed to elicit rabbit antibody response to the L form antigen. The greatest number of human sera containing complement-fixing antibody to L form antigen (69·0%) were found among 16 patients who had experienced recent group A streptococcal infections. 51% of 62 naval recruits among whom such infections had previously been found with great frequency were also positive. 40 recruits with virus infections which required hospitalization gave 9 (22·5%) positive results. Other selected groups studied as normal controls gave positive results in 3 of 44 serum samples.

Attempts to obtain complement-fixation with similar extracts of intact or disrupted bacterial cells, cell wall, or cytoplasm of group A streptococci gave completely negative results against L-positive human sera. Similarly only L forms and not the bacterial cells or the fractions thereof were able to adsorb out the complement-fixing antibody from a human serum.

[The paradoxical result that the L form antibody was produced in response to the bacterial cells in which it was not possible to demonstrate the antigen may well be due to the extraction method. The L form is very fragile, even to washing with saline [PANOS *et al.*, *ibid.*, 1960, v. 35, July]. All the bacterial cell fractions were prepared by sonic disruption of the organisms but it is not stated if the antigen is stable to such treatment.] *H. Gooder*

CHESBRO, W. R. & EVANS, J. B. **Factors affecting the Growth of Enterococci in Highly Alkaline Media.** *J. Bacteriology.* 1959, Dec., v. 78, No. 6, 858–62, 4 figs.

The authors investigated the factors affecting the growth of enterococci in alkaline medium, as the ability to grow in media at *p*H 9·6 is widely used as a test for the identification of *Streptococcus faecalis* but sometimes gives erratic results.

Enterococci were found to grow poorly in a tryptone-yeast-glucose medium at a *p*H above 9·0 but between *p*H 8·0 and 9·0 growth was stimulated by added carbonate. Glycine and the D-isomer of some amino-acids were relatively toxic in this medium at high *p*H. Oleate stimulated growth and reduced the toxicity of added glycine.

In view of these findings the authors suggest that a satisfactory medium for testing enterococci is a tryptone-yeast-glucose medium containing 0·05M carbonate and 0·05% Tween 80 or Span 80 at a *p*H 10·0.

M. Patricia Jevons

HEIDELBERGER, M. **The Immunological Specificity of Type II Pneumococcus and its Separation into Partial Specificities. II.** *J. Exper. Med.* 1960, Jan. 1, v. 111, No. 1, 33–43. [29 refs.]

The principal determinant of pneumococcal type II serological specificity is a capsular polysaccharide (SII) composed of D glucose, L-rhamnose and D-glucuronic acid. The last named is in a form containing non-reducing end groups. By means of quantitative precipitin analysis at 0°C. with polysaccharides and gums containing glucuronic acid or 4 methylglucuronic acid or both it has been possible to investigate the partial specificities of the antibodies in type II pneumococcal sera directed towards such groupings. Considerable variation was shown both in the reactivity of the polysaccharide and in the antibodies in the sera of 3 different horses immunized with the same antigen. The 4-O-methyl substituent on the glucuronic acid residues in a gum often appears to diminish cross precipitation with antibodies to SII.

[For Part I, see this *Bulletin*, 1956, v. 31, 760.]

H. Gooder

OPARA-KUBINSKA, Z. **Investigations on Bacterial Transformations. I. Influence of Centrifugation on the Transformation Ability ("Competence") of *Diplococcus pneumoniae* Cells.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1959, v. 7, No. 11, 433–7. **II. Influence of Tween 80 on the Transformation of Streptomycin-Resistance of Pneumococci.** *Ibid.*, 439–43.

I. The effect of a transforming principle for streptomycin resistance on a non-encapsulated pneumococcus was tested with and without preliminary centrifugation and resuspension of the receptor cells. The number of transformations was almost always greater in the centrifuged samples. It is suggested that this effect was in some way linked with the aggregation produced by centrifugation.

II. The addition of Tween 80, in concentrations of 0·04% or more, to the transforming principle, inhibited transformation. The addition had to be made during the period before the penetration of the transforming principle into the cell. *R. E. O. Williams*

LAURELL, Anna B. **Neuraminidase-Like Factors in Cultures of Pneumococci, Alpha-Streptococci and *Pasteurella pseudotuberculosis*.** *Acta Path. et Microb. Scandinavica.* 1959, v. 47, No. 2, 182–90, 3 figs. [12 refs.]

CATLIN, B. W. **Interspecific Transformation of *Neisseria* by Culture Slime containing Deoxyribonucleate.** *Science.* 1960, Feb. 26, v. 131, 608–10. [18 refs.]

"Genetic change of *Neisseria meningitidis* is elicited by deoxyribonucleate preparations obtained from *N. sicca*. Such interspecific transformation is effected not only by deoxyribonucleate obtained from cells by conventional methods but also by crude deoxyribonucleate-containing slime which accumulates without experimental intervention in some cultures incubated for a period as short as 44 hours."

GOLDBERG, J. **Studies on Granuloma Inguinale. IV. Growth Requirements of *Donovania granulomatis* and its Relationship to the Natural Habitat of the Organism.** *Brit. J. Venereal Dis.* 1959, Dec., v. 35, No. 4, 266–8. [13 refs.]

"*Donovania granulomatis* has hitherto been reported to grow only on material containing egg yolk material. Evidence is presented to indicate that two factors are necessary for growth:

"(1) A low oxidation-reduction potential which can be satisfied by the use of a thioglycollate medium;

"(2) A factor or factors found in egg for which may be substituted the enzymatic digests of bovine albumin or soya meal.

"Acid hydrolysis of these materials destroys this factor. Presumptive evidence is presented to indicate that this factor is probably a peptide. These findings along with the previously published serological relationships between *D. granulomatis* and members of the Enterobacteriaceae, strengthen the idea of a faecal habitat of *D. granulomatis*."

JEFFERIES, Mildred B., HARDY, A. V. & SCHNEIDER, N. J. **The Relative Efficacy of Culture Media for the Isolation of *M. tuberculosis* from Clinical Material.** *Amer. Rev. Respiratory Dis.* 1960, Feb., v. 81, No. 2, 259–65.

In this comparison Löwenstein-Jensen medium (LJ) was compared with Tarshis penicillin blood agar medium, American Trudeau Society egg medium (ATS), Peizer TB medium (Difco), Middlebrook 7H9 Agar A medium and Peizer's semi-synthetic autoclavable medium. 27,271 specimens were cultured and they consisted mainly of sputa but included some urine, faeces and gastric washings. All the specimens were treated with trisodium phosphate and the deposits inoculated onto 2 tubes of LJ medium and 1 tube of 1 of the other media. As it was not feasible to compare all the media together, the LJ medium served as the standard and each comparison consisted of approximately 5,000 specimens. The sequence of inoculating the tubes of media alternated between an LJ slope and the test medium. The results are shown in the table below.

The LJ medium proved to be the best, although the difference between the results with it and the ATS medium was not statistically significant; the results could also be read earlier with these 2 media than with the others. Analysis of the result of inoculating a 3rd tube, *i.e.* a 2nd tube of LJ medium, showed that the number of positive results was only increased from 5·2 to 5·4%. *S. R. M. Bushby*

Test Medium (TM)	Total No. of specimens	% positive	Distribution of positive results		
			% positive on both media	% positive on LJ and negative on TM	% negative on LJ and positive on TM
Penicillin blood agar	5,849	8·9	76·3	17·8	5·9
ATS	6,161	4·4	77·1	13·1	9·8
Peizer TB	5,099	4·5	64·7	29·1	6·2
Middlebrook 7H9 Agar A	5,094	3·8	63·6	32·3	4·1
Semi-synthetic autoclavable	5,068	4·1	44·4	52·7	2·9

COLETSOS, P. J., with the collaboration of E. ORIOT, N. DE REGEL & M. G. MACHAVOINE. Revelation et multiplication *in vitro* du bacille de la tuberculose en "état de quiescence" considéré comme non viable. Déductions d'ordre épidémiologique. [**Detection and Multiplication *in vitro* of Tubercle Bacilli in an Apparently Non-Viable Quiescent State. Epidemiological Implications**] *Bull. Acad. Nat. Méd.* 1959, v. 143, Nos. 21, 22 & 23, 479–84, 3 figs.

In the first part of this communication the value of the medium which was developed at the Pasteur Institute and which consists of egg, metal catalysts, amino acids and sodium pyruvate plus an extract of monkey liver is illustrated by photographs. Pathological specimens from patients treated with antibiotics and containing acid-fast bacilli that did not grow or grew only a few colonies on Jensen medium, yielded a profuse growth of tubercle bacilli on the Pasteur Institute medium.

In the second part an experiment is described in which an attempt was made to see whether tubercle bacilli would pass into a quiescent state when exposed *in vitro* to PAS and, if so, whether they would grow on the medium containing monkey liver. The tubercle bacilli were from a patient who had been treated with PAS but they were sensitive to 0·1 μgm. PAS per ml. They were grown on a series of tubes of egg medium containing concentrations of PAS ranging from 0·01 to 10 μgm./ml. and at intervals during the incubation time PAB was added to the medium. In the series of tubes to which the PAB was added on the 2nd to 4th day, growth greater than that on the PAS-free control tube occurred in the presence of 0·01–2 μgm. PAS per ml., and growth equal to it occurred on the

medium containing 10 μgm. PAS per ml. When the PAB was added after 21 or 30 days' incubation there was still some reversal of the PAS activity for growth occurred in the presence of 0·1 μgm. PAS per ml. and, when the interval was 21 days, to a lesser extent with 1 μgm./ml.; however, when monkey liver was added with the PAB, not only was the growth increased slightly in the presence of these concentrations of PAS but it now occurred in the presence of 5 μgm./ml. when the interval was 21 days and of 2 μgm./ml. when it was 30 days.

This result is interpreted as showing that tubercle bacilli can be encouraged *in vitro* to enter a quiescent state in which they will not multiply on ordinary media, and therefore it can be assumed that tubercle bacilli enter a similar state *in vivo*.

S. R. M. Bushby

ERLICH, H. **Rapid Identification of Mycobacterial Colonies. I. The Auramine Test.** *Amer. Rev. Respiratory Dis.* 1960, Feb., v. 81, No. 2, 218–25.

The author claims to have developed a new reagent, alkaline-auramine, for staining the colonies of mycobacteria. 3 methods are described: in the first the growth is rubbed into a half-inch disc of filter paper, impregnated with auramine, and a positive reaction occurs if after a little 0·5 N NaOH is added the disc becomes bright yellow; in the second, an *in situ* method, a mixture of alcoholic auramine solution and NaOH are poured over an oleic-acid-albumin agar culture, and colonies which develop a brilliant yellow colour, persisting for more than 1 minute, are regarded as auramine-positive; in the third method the positive discs of the first method are viewed under ultra-violet light after they have been incubated for 2 hours at 37°C. and their colour noted.

In their preliminary study with these methods, 59 strains of atypical mycobacteria and 43 strains of tubercle bacilli were tested. The tubercle bacilli were positive by all 3 methods, and fluoresced a greenish colour. The 14 strains of photochromogens were also positive but fluoresced either greenish or yellow orange. The 10 scotochromogens were all positive by the disc method, but 1 was negative and 2 only doubtfully positive by the *in situ* method, and although 6 strains fluoresced green, the other 4 were very faint or failed to fluoresce. Of the 15 strains of non-photochromogens, 3 were weakly positive by the disc method, and the other 12 were definitely positive; 13 were positive but 2 were only weakly positive by the *in situ* method, and they fluoresced greenish and yellow orange. 14 strains of various other mycobacteria were examined and these were mostly rapid growing saprophytes; 2 showed "cording" and one of these was auramine positive; the fluorescence by these strains varied from green to orange yellow and some were non-fluorescent.

All these strains were tested by the neutral-red method and the positive reactions paralleled those by the auramine disc and *in situ* methods. Cording could easily be detected after staining in the *in situ* method by microscopical examination of the colony after covering it with a cover slip.

The staining of the bacilli by the alkaline-auramine is believed to be due to the mycolic acid in the bacilli.

S. R. M. Bushby

LYANG, K. W. **Studies on the Interaction between Host Cell and Parasite. I. Morphologic Studies of Lung Tissue cultured** *in vitro*. *Amer. Rev. Respiratory Dis.* 1960, Feb., v. 81, No. 2, 200–205, 7 figs. [14 refs.] **II. The Reaction of Pulmonary Cells cultured** *in vitro* **to Virulent Tubercle Bacilli.** *Ibid.*, 206–12, 8 figs. [19 refs.]

I. Embryonic guineapig lung was used for these studies. Small pieces of lung from embryos 40 to 50 days old were trypsinized and the cells grown on glass in special tissue culture chambers. The fluid medium (60% Tyrode's solution, 30% horse serum and 10% chick embryo extract) was changed every 48 hours. 2 cultures were fixed and stained each day for 2 weeks. 3 types of cells were identified in the cultures—epithelial, macrophage and spindle cells. The epithelial cells, assumed to arise from the alveolar epithelium, formed sheets and islands. These cells survived well but no mitosis was observed. The spindle cells (derived from capillary endothelium and from fibroblasts) formed strands and showed mitosis. The macrophages were the most unstable of the 3 types of cells, gradually becoming degenerate and showing no mitosis.

II. Studies on the interaction between these cells and virulent tubercle bacilli were undertaken by adding suspensions of human bacilli (strain Kurono) or bovine bacilli (strain Ravenel) to the tissue cultures on the second or third day. 2 cultures of each strain were fixed and stained every day for 2 weeks. Although all 3 cell types phagocytosed tubercle bacilli the macrophages were by far the most active. The infected macrophages degenerated rapidly and the intracellular tubercle bacilli appeared to be granular and did not multiply. In contrast to the macrophages, the infected epithelial cells remained healthy and the intracellular bacilli multiplied, forming the characteristic serpentine cords. The few infected spindle cells also remained healthy but the ingested bacilli did not form cords.

R. J. W. Rees

GRAY, D. F. **Fate of Tubercle Bacilli in Early Experimental Infection of the Mouse.** *J. Hygiene.* 1959, Dec., v. 57, No. 4, 473–83, 9 figs. on 3 pls. [13 refs.]

Some workers have reported that tubercle bacilli cannot be seen after Ziehl-Neelsen staining in the tissues of mice 24 hours after injection [this *Bulletin*, 1948, v. 23, 846]. In the present study, groups of 60 mice were injected intranasally and intravenously with H37Rv and sections of the lungs of half of the animals stained with auramine-rhodamine and examined by fluorescence microscopy. Homogenates of the lungs of the other half of the animals were made and these

were examined quantitatively for acid-fast bacilli in smears and for viable tubercle bacilli. These examinations were made 2 hours, 24 hours and then daily for 7 days after infection. For the intranasal experiments, C57 Black mice and a local [Melbourne] strain of mice were used and as no difference was found between them, only the local strain was used in the intravenous experiments.

In contrast to the reports by other workers, tubercle bacilli were demonstrated and cultured during each of the 7 days after intranasal injection, and an apparent initial increase of about 7-fold was observed during the first day followed by a quiescent phase, or one of slight multiplication, lasting till the third or fourth day. The initial apparent increase was considered to be due to the dispersal of the aggregates of bacilli through phagocytic activity. Varying the decolorization time of the stained bacilli showed that they became less acid-fast during the lag phase of multiplication.

Although with intravenous injection the number of bacilli in the lungs was more variable in the individual mice than with the intranasal injection, the general picture was the same as that described above.

These experiments therefore revealed no suggestion of an eclipse phase, but the decrease in acid-fastness suggests that the claims for such a phase are due to the bacilli becoming less easily demonstrable by the Ziehl-Neelsen stain. The authors suggest that the lag phase in multiplication is due to a need for the bacilli to become adjusted to an intracellular existence.

S. R. M. Bushby

ROBSON, J. M. & SULLIVAN, F. M. **Immunity in Tuberculosis.** *Brit. J. Dis. Chest.* 1960, Jan., v. 54, No. 1, 3–21. [Numerous refs.]

This review consists of 13 sections and the first 9 are devoted almost entirely to the investigations made during the last decade into the value of vaccination for stimulating immunity against the tubercle bacillus. Attention is first drawn to the conflicting results of experiments aimed at showing non-specific stimulation of immunity by non-tuberculous and tuberculous antigens, and the authors then make the following generalizations about the immunity produced by vaccination or infection with tubercle bacilli: (1) immunity has been demonstrated in 14 species of animals, including man, and, except possibly for mice, the immunity is associated with a development of hypersensitivity; (2) virulent strains confer the greater immunity, but mycobacteria, other than the tubercle bacillus, confer some degree of protection against tuberculosis; (3) the response of a vaccine is proportional to the dose and in order to confer a similar degree of protection the dose of dead bacilli must be larger than that of living ones; (4) the relative effectiveness of the different parenteral routes or of oral routes of vaccination is still in doubt; (5) the speed with which experimental immunity develops is not known with certainty because the immunity continues to develop after challenge with virulent bacilli, and it is also unknown whether the duration of immunity is related to the duration that the living vaccine remains viable in the host; (6) the degree of immunity demonstrable depends upon the size of the challenge dose; (7) hypersensitivity is not a necessary prerequisite for the production of immunity, and the 2 states can be dissociated.

From a discussion of some of the evidence that humoral factors play a role in immunity, the conclusion is reached that there is still no conclusive evidence that they are important. As far as the role of cellular factors are concerned there is little doubt that macrophages from immune animals have a restraining effect on the multiplication of tubercle bacilli.

Of the other factors that may be involved in the development of immunity, decreased oxygen supply *in vivo* undoubtedly affects the multiplication of the tubercle bacillus, but it is difficult to draw any general conclusion from the many experiments designed to determine the exact role of reduced oxygen tension in the mechanism of tuberculous immunity. High local concentrations of organic acid, especially lactic acid, may inhibit the multiplication of tubercle bacilli for such acids are toxic to the bacillus. Sex hormones have been reported to exert an effect on the development of experimental tuberculosis but only when given in large doses, and in man it would seem that the response to vaccination is independent of sex.

S. R. M. Bushby

VINCZE, E., SCHWEIGER, O. & VANDRA, Edit. **Further Observations on the Isoniazid-Resistance, Catalase Activity, and Virulence of** *M. tuberculosis.* *Acta Tuberculosea Scandinavica.* 1960, v. 38, No. 1, 26–39, 9 figs. (4 on 4 pls.) [21 refs.]

In this study a catalase-negative strain of tubercle bacilli resistant to 20–80 μgm. isoniazid per ml. and a catalase-positive strain resistant to 10–20 μgm. isoniazid per ml. were injected into 8–10 guineapigs, before and after being grown twice more on an isoniazid-containing medium. At fortnightly intervals 2 guineapigs from each group were killed and cultures made from the draining-lymph gland, the spleen and the liver of each. Guineapigs were also inoculated with H37Rv and a catalase-negative variant, resistant to 80–100 μgm. isoniazid per ml., singly and as an equal-part mixture, and these animals were similarly examined.

The recoverability of the isoniazid-resistant strains was found to decrease progressively so that by the 8th week they were seldom recovered; this decrease was less marked with the catalase-negative than with the catalase-positive strains. The mixture of sensitive and resistant H37Rv behaved similarly to the sensitive strain, *i.e.* its recoverability increased with time.

The recovered organisms usually showed the same catalase activity as the parent strain, and although they were mainly of the same isoniazid-resistance, some of the bacilli of the catalase-positive strain showed some decrease in resistance in spite of the parent strain having been grown twice more in the presence of the drug.

The catalase-negative strains were the less virulent, shown by a greater tendency for the lesions to regress, and in discussing these results the authors suggest that the appearance of catalase-negative strains in specimens from patients should be interpreted as an indication that no more improvement is likely to result from continuing isoniazid therapy. *S. R. M. Bushby*

GRUMBACH, Francoise & RIST, N. Comparaison de l'activité antituberculeuse expérimentale de la thiocarbanidine et de l'éthioniamide. [**Comparative Study of the Experimental Antituberculous Activity of Thiocarbanidine (THC) and Ethioniamide (1314 Th).** *Ann. Inst. Pasteur.* 1960, Mar., v. 98, No. 3, 373–82. [19 refs.]

The English summary appended to the paper is as follows:—

"In spite of the presence of a common chain ($CSNH_2$), the mechanism of activity of the two products is very different. Both are active in mice tuberculosis. For an abortive treatment of short duration, the minimal active dose of THC is lower than that of 1314 Th. On the other hand, THC has only a low activity as a curative treatment. Associated with isoniazid or 1314 Th, THC does not prevent the appearance of resistant bacilli to one of these antibiotics. The inactivity of THC under these conditions seems to be due to a poor absorption by the animal body."

GRAY, J. E., STERN, K. F. & RHULAND, L. E. **Modification of Experimental Murine Tuberculosis by an Antimicrobial Agent, Streptovaricin.** *Amer. Rev. Respiratory Dis.* 1960, Feb., v. 81, No. 2, 226–34, 10 figs. [10 refs.]

The effect of streptovaricin on experimental tuberculosis was assessed by following the bacillary population and the histopathological changes in the lungs and spleen of heavily infected mice. These investigations were undertaken because earlier studies [this *Bulletin*, 1957, v. 32, 802] had shown that 10 days' treatment with streptovaricin resulted in greater survival in mice than with comparable doses of isoniazid and streptomycin. 4 groups of infected mice were compared: Group A, daily treatment with streptovaricin for 152 days; Group B and D, daily treatment for 10 and 70 days respectively; and Group C untreated. The same daily dose of streptovaricin (400 mgm./kgm. body weight, orally) was given from the first day of infection to all the treatment groups.

Survival was prolonged equally in the 3 treatment groups, whereas the populations of viable tubercle bacilli in the lungs and spleens differed. The infection was rapidly suppressed in the animals receiving continued treatment (Group A), but a few viable bacilli persisted in the lungs and spleens until the 152nd day. Organisms recovered after 128 days were resistant to streptovaricin. There was a small increase in the number of viable organisms in the tissues of animals after treatment was discontinued on day 70 (Group D). On the other hand, interruption of treatment at 10 days (Group B) was followed by a rapid rise in the population of bacilli, reaching a high level by the 6th week. The bacillary population then remained at a high level over a period of 152 days. The high population of viable tuberculi bacilli did not result in death of the mice and the development of host resistance was considered to be responsible for the prolonged survival of this group of animals. The cellular response, consisting of foam cells and lymphocytes, was consistent with this hypothesis. *R. J. W. Rees*

GORDON, Ruth E. & MIHM, Joan M. **A Comparison of Four Species of Mycobacteria.** *J. General Microbiol.* 1959, Dec., v. 21, No. 3, 736–48, 8 figs. on 2 pls. [20 refs.]

"Expanded descriptions of *Mycobacterium phlei* Lehmann & Neumann, *M. smegmatis* (Trevisan) Lehmann & Neumann, *M. fortuitum* Cruz, and the species tentatively designated as *M. rhodochrous* (Overbeck) Gordon & Mihm are presented. These characterizations are based on 40, 95, 80, and 79 strains respectively, upon which 39 different tests and observations were made."

BÖNICKE, R., DITTMAR, W. & LISBOA, B. P. Über das Vorkommen von Acylamidasen in Mycobakterien. II. Mitteilung: Der enzymatische Abbau von Harnstoff (Urease). [**On the Presence of Acylamidase in Mycobacteria. 2nd Communication: The Enzymatic Fermentation of Urea**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 3, 380–93, 5 figs.

MICHEL, G. Étude des lipides de *Mycobacterium marianum*. [**Study of the Lipids of** *Mycobacterium marianum*] *Bull. Soc. Chimie Biol.* 1959, v. 41, No. 12, 1649–69, 2 figs. [33 refs.]

HART, P. D'A. & VALENTINE, R. C. **Elongation of a Leprosy Bacillus (*Mycobacterium lepraemurium*) in a Cell-Free Medium.** [Correspondence.] *Nature.* 1960, Jan. 2, v. 185, 58–60.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 601.]

AGARWAL, S. C. & NASMYTH, P. A. **Some Peripheral Actions of Diphtheria Toxin.** *J. Physiology.* 1959, Oct., v. 147, No. 3, 511–20, 4 figs. [10 refs.]

Pursuing the problem of the ultimate site of action of diphtheria toxin, the authors suggest that this is located in the vascular system. There is a general tendency to dilatation of the capillary blood vessels.

They find no evidence of diminished production of vasoconstrictor amines but consider that the toxin may operate through diminishing sensibility to these and they discuss the possibility that the toxin effects its damage by altering the permeability of the cell membrane to potassium ions in some tissues, notably the vascular system. *J. W. McLeod*

Munoz, J., Ribi, E. & Larson, C. L. **Antigens of *Bordetella pertussis*. I. Activities of Cell Walls and Protoplasm.** *J. Immunology.* 1959, Nov., v. 83, No. 5, 496–501, 2 figs. [21 refs.]

Bordetella [*Haemophilus*] *pertussis* organisms which had grown on Bordet-Gengou medium during a 48-hour incubation period at 37°C. were suspended in cold physiological saline and disintegrated with glass beads in a Mickle disintegrator. Centrifugation of the disintegrated cells produced a supernatant fluid containing protoplasm and further differential centrifugation separated the cell wall suspension from the disintegrated cells. The preparations of protoplasm and cell walls were tested for (a) their ability to immunize mice against a lethal pertussis challenge dose, (b) their ability to sensitize mice to histamine, and (c) their toxic properties.

It was found that the heat labile toxin was mainly present in the protoplasm whereas the protecting antigen and the histamine sensitizing factor were located principally in the cell wall. *F. T. Perkins*

Walecki, H. Aglutynacyjnośc szczepów *H. pertussis* z surowicą *H. parapertussis*, jako wskaznik formy gładkiej. [**Agglutinability of *H. pertussis* Strains with Anti-*H. parapertussis* Serum as an Index of Smooth Form**] *Med. Dośw. i Mikrob.* Warsaw. 1959, v. 11, No. 4, 313–19. [26 refs.]

The English summary appended to the paper is as follows:—

"Sixty-eight laboratory and freshly isolated *H. pertussis* strains were examined in reference to their agglutinability with anti-*H. pertussis* and *H. parapertussis* standard sera. It was found that the strains agglutinating to the equal titre with anti-*H. pertussis* serum may present various titres of agglutination with anti-*H. parapertussis* serum. Orientation studies on mice showed that with the increase of paraagglutination titre the protective potency of a strain is lowered. Therefore it seems to be useful to take under consideration agglutination titre of *H. pertussis* strain with anti-*H. pertussis* serum for the selection of strains in the production of pertussis vaccine."

Preston, N. W. **Factors influencing the Assay of the Histamine-Sensitising Factor of *Haemophilus pertussis*.** *J. Path. & Bact.* 1959, July, v. 78, No. 1, 217–24, 1 fig.

It was found that the histamine sensitizing factor (HSF) of pertussis vaccine could be estimated qualitatively by injecting mice with serial dilutions of vaccine and challenging with a constant dose of histamine. It was necessary, however, to use female mice of limited weight-range (22–26 gm.) and the histamine dihydrochloride disolved in buffer (*p*H 7·4) was probably better than acid phosphate. *F. T. Perkins*

Zinnemann, K. *Haemophilus influenzae* **and its Pathogenicity.** *Ergebn. Mikrobiol. Immunitätsf.* 1960, v. 33, 307–68, 13 figs. [Numerous refs.]

Munoz, J. & Anacker, R. L. **Anaphylaxis in *Bordetella pertussis*-treated Mice. II. Passive Anaphylaxis with Homologous Antibody.** *J. Immunology.* 1959, Nov., v. 83, No. 5, 502–6. [14 refs.]

Mouse antibody used to induce passive anaphylaxis was produced in mice by intraperitoneal injection of hen's egg albumin in Freund's adjuvant. The ascites fluid that accumulated in the peritoneum was found to contain appreciable amounts of antibody. Passive anaphylaxis was induced by a single intraperitoneal inoculation of 2×10^9 *Bordetella* [*Haemophilus*] *pertussis* cells 4 days before an intraperitoneal injection of a sensitizing dose of mouse antibody. 5–6 hours after injection of the antibody the mice were challenged intravenously with 0·5 mgm. of egg albumin.

It was found that fatal passive anaphylaxis could be induced in pertussis-treated mice with as little as 6–7 μgm. of mouse antibody nitrogen. Although normal mice can be sensitized to fatal anaphylaxis with mouse antibody a much larger dose is required than for mice treated with *B. pertussis*. No latent period was observed after intravenous injection of antibody since mice could be fatally shocked as early as 5–10 seconds and as late as 6 days after administration of the antibody. Symptoms were observed 13 but not 21 days after the antibody was given. *F. T. Perkins*

Munoz, J. & Anacker, R. L. **Anaphylaxis in *Bordetella pertussis*-treated Mice. III. Passive Cutaneous Anaphylaxis.** *J. Immunology.* 1959, Dec., v. 83, No. 6, 640–44. [13 refs.]

Passive cutaneous anaphylaxis (PCA) was induced in mice and rats by intradermal injection of antibody prepared against hen's egg albumin followed 3 hours later by a sensitizing intravenous injection of hen's egg albumin (Ea) mixed with Evans blue dye. Finally $\frac{1}{2}$ to 1 hour later the animals were killed and the inner surface of the injected skin was examined for circular areas of dye accumulation.

Antibody to Ea was produced in both rabbits and mice and it was found that approximately 50 times more rabbit anti-Ea antibody nitrogen than mouse anti-Ea antibody nitrogen was necessary to give minimal PCA in mice. With the homologous antibody PCA can be induced in mice as early as 15 minutes and as late as 6 hours after injection of antibody.

Despite the close phylogenetic relationship of mice and rats, approximately as much mouse antibody as rabbit antibody is required to sensitize the rat to PCA.

Pretreatment of mice with *Bordetella* [*Haemophilus*] *pertussis* organisms did not enhance PCA in the mouse sensitized with either mouse or rabbit anti-Ea antibody although it is well known that these organisms increase their sensitivity to active and passive anaphylaxis [see also this *Bulletin*, 1959, v. 34, 88; Munoz and Anacker, above]. *F. T. Perkins*

JEFFRIES, L. **Novobiocin-Tetrathionate Broth: a Medium of Improved Selectivity for the Isolation of Salmonellae from Faeces.** *J. Clin. Path.* 1959, Nov., v. 12, No. 6, 568–71.

Salmonellae were found to be resistant to relatively large doses of novobiocin, whereas, of all the Gram-negative intestinal bacilli tested, members of the *Proteus* group were found to be the most sensitive. Tetrathionate broth containing 40 μgm. novobiocin/ml. medium proved to be superior to plain tetrathionate broth as an enrichment medium for the isolation of salmonellae from faeces artificially infected with known members of the salmonella and proteus groups of organisms.

Although the experiments described in this paper suggest that the addition of novobiocin to liquid enrichment media would improve its selectivity for salmonella organisms, the results of extensive controlled trials with naturally infected faeces must be awaited before the value of this selective medium can be properly assessed. *H. J. Bensted*

SCHLOSSHARDT, Johanna. Untersuchungen über die Entstehung von T-Antigenen im S-R-Formenwechsel bei Salmonellen. [**Investigations on the Origin during S-R Variation of T Antigens in *Salmonella* Cultures**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 2, 176–85, 1 fig. [10 refs.]

TIMAKOV, V. D., KUDLAI, D. G., PETROVSKAIA, V. G., KORNEEVA, A. M. & BOGATYREVA, S. A. **A Comparative Immuno-Chemical Study of Strains of *Salmonella typhosa* of differing Virulence.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 2, 27–33, 2 figs. [11 refs.] [Translated from Russian.]

This paper is not, in fact, concerned with *Salmonella typhi*, but with the effect of streptomycin on *Salm. paratyphi B* in inducing the development of variants of reduced virulence and also variants which are avirulent. The authors describe changes in the chemical constitution of these variants as compared with the parent strain. It is stated that as the virulence decreases the organisms show an increase in their ribonucleic acid content. Glucosamine is decreased; there is more free lipid, but the amount of bound lipid is less. It is suggested that certain antigenic changes found in the avirulent variants are the results of an alteration in the distribution of components of the somatic antigen-complex, but evidence is not provided to support this. *H. J. Bensted*

ZUYEV, A. S. **A Bacillary Diagnostic Vi Antigen for the Detection of Chronic Carriers of Typhoid Bacilli.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 2, 61–8. [12 refs.] [Translated from Russian.]

The relative instability of the Vi antigen in bacterial suspensions employed for the detection and measurement of Vi agglutinins in the sera of persons with a history of typhoid fever has been well recognized for more than 20 years. Many methods have been introduced with the object of stabilizing the antigen in agglutinable suspensions, but long experience has shown that none of the methods has proved sufficiently reliable to enable diagnostic Vi antigens to be used for the quantitative agglutination test without the inclusion of a standard Vi serum, as a vital control, in every batch of tests put up. The strain of typhoid bacillus, almost universally, used for the preparation of this Vi antigen has been *Salmonella typhi* Vi I (Bhatnagar). This strain is generally very sensitive to the action of Vi agglutinins, but because of its S-R tendency the greatest care is necessary for the production of agglutinable suspensions. On occasions a simple suspension in buffered formal-saline may remain stable for many months and, even though the additional treatment with calcium chloride (the method favoured by the author of this paper) may appear to yield more consistent results, it is still essential to employ a standard Vi serum in all tests. Treatment with calcium chloride is not a new technique; it was examined by the reviewer some years ago with rather disappointing results. This article does not stress the importance of the standard Vi serum for controlling the agglutinability of the bacillary suspension. *H. J. Bensted*

GORYSHINA, L. V. **Experimental Study of the Composition of the Vi Antigens of *Escherichia coli* and Strains of *Salmonella typhosa* by the Method of Gel Diffusion.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 2, 96–101, 7 figs. [Translated from Russian.]

The author employed 4 strains of Vi-containing organisms, *Escherichia coli* 5396/38, *Ballerup* 6021, a Vi strain of typhoid bacillus and the classical Vi I (Bhatnagar) strain and used a Boivin type extract against various antisera in conventionally conducted gel diffusion procedures. The results clearly demonstrated the single identity of the Vi components of the 3 organisms and the separate identity of the O antigen complex of *E. coli*, *Ballerup* and the typhoid strains. *H. J. Bensted*

VAN OYE, E. Les Salmonellae du Congo belge (Septième Rapport). [**Salmonellae of the Belgian Congo (Seventh Report)**] *Ann. Soc. Belge de Méd. Trop.* 1959, Oct. 31, v. 39, No. 5, 717–23. [12 refs.]

The English summary appended to the paper is as follows:—

"In this 7th report on the *Salmonellae* of the Belgian Congo and Ruanda-Urundi which follows on the six published previously, a description is given of the 11 serotypes which have been identified for the first time since January 1958. Five of these are new to science, notably *S. inganda*=6,7 : z_{10} : 1,5—*S. ipeko*=9,12 : c : 1,6—*S. bolombo*=3,10 : z_{38} :——*S. bukavu*=1,40 : 1,z_{28} : 1,5 and *S. ngozi*=48 : z_{10} : 1,5.

"Some statistical information is given on the relative frequency of the most important *Salmonellae* isolated in 1,000 human cases."

YAKHNINA, N. A. & KUZNETSOVA, N. S. **The Value of Experimental Keratoconjunctivitis as a Model for studying Immunity in Dysentery.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 2, 123–7. [Translated from Russian.]

There have been several papers in the last 2 years or so by workers in Eastern Europe on the keratoconjunctival reaction in guineapigs to the installation of shigella organisms and the nature of the immune responses [this *Bulletin*, 1958, v. 33, 66, 264, 689, 690; 1959, v. 34, 567, 673; 1960, v. 35, 191]. This paper does not appear to offer information that is significantly different from that given in previously published papers. As it is not properly documented in the English version it is not possible to check references. *H. J. Bensted*

GORIACHKINA, N. S. **A Study of the Lytic Action of Dysentery Phages in Mice infected with** *Shigella flexneri*. *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 2, 75–80. [Translated from Russian.]

This article reports the testing of the lytic action of phages of the Flexner group of dysentery bacilli in groups of mice inoculated with organisms belonging to different serological types of *Shigella flexneri*. The results as set out would appear to indicate that these phages exhibit a distinct specificity of action. The author identifies his serological types as V, W, X, etc. which, it is presumed, refers to ANDREWES system of nomenclature. His active phage, which he designates WXZ, is specific for the serotype W; phage WXZ injected into mice 24 hours before infecting them with Flexner type W showed a 10-fold rise in phage titre whereas a similar group of mice injected with phage WXZ 24 hours before infection with serotype V showed no increase in titre. *H. J. Bensted*

i. COETZEE, J. N. **The Late Lactose-Fermenting Property of** *Shigella sonnei*. *South African J. Lab. & Clin. Med.* 1959, Sept., v. 5, No. 3, 170–79, 3 figs. [23 refs.]

ii. ——. **The Back Mutation Rate of Lactose-Positive Variants of** *Shigella sonnei*. *Ibid.*, 180–86, 1 fig.

i. "Proof of the mutational origin of lactose-positive cells from wild-type *Shigella sonnei* is presented and the rate of mutation determined."

ii. "The mutational origin of wild-type cells from lactose-positive variants of *Shigella sonnei* was established by means of fluctuation tests. The high mutation rate involved was determined by means of continuous culture experiments."

LACKS, S. & GROS, F. **A Metabolic Study of the RNA-Amino Acid Complexes in** *Escherichia coli*. *J. Molecular Biol.* London. 1959, Dec., v. 1, Nos. 4/5, 301–20, 12 figs. [25 refs.]

HALL, C. E. & SLAYTER, H. S. **Electron Microscopy of Ribonucleoprotein Particles from** *E. coli*. *J. Molecular Biol.* London. 1959, Dec., v. 1, Nos. 4/5, 329–32, 1 fig. & 1 pl.

TISSIÈRES, A. **Some Properties of Soluble Ribonucleic Acid from** *Escherichia coli*. *J. Molecular Biol.* London. 1959, Dec., v. 1, Nos. 4/5, 365–74, 4 figs. & 3 pls. [20 refs.]

TORRIANI, Annamaria. **Influence of Inorganic Phosphate in the Formation of Phosphatases by** *Escherichia coli*. *Biochim. et Biophys. Acta.* 1960, Mar. 11, v. 38, No. 3, 460–69, 5 figs. [14 refs.]

GAREN, A. & LEVINTHAL, C. **A Fine-Structure Genetic and Chemical Study of the Enzyme Alkaline Phosphatase of** *E. coli*. **I. Purification and Characterization of Alkaline Phosphatase.** *Biochim. et Biophys. Acta.* 1960, Mar. 11, v. 38, No. 3, 470–83, 13 figs. [33 refs.]

WAISBREN, B. A., ERLANDSON, A. L. & FISHER, M. W. **Severe Infections in Adults caused by Mouse-Virulent Strains of** *Escherichia coli*. *New England J. of Med.* 1959, Nov. 19, v. 261, No. 21, 1056–8. [20 refs.]

Escherichia coli was isolated from the blood, a periurethral abscess and the sputum respectively, of 3 severely ill patients, 2 of whom died. The strains isolated were reported as highly virulent for mice. They were not identified in accordance with their O-antigen formulae but their LD50, as measured by the mucin-mouse-virulence test, showed them to be many times more virulent than such recognized enteropathogenic strains as: O 55, O 111, O 127 or O 86. Whereas the strains isolated from cases of epidemic diarrhoea in children had an LD50 in the mucin test of 40 bacterial cells upwards, mice succumbed from as few as 2 bacteria of the 3 strains under discussion.

[In the absence of information about the antigenic structure of these strains of *E. coli* it is difficult to offer any comment. It would have been of considerable interest to know whether, in addition to their O-antigen formulae, any of the strains were carrying the Vi antigen. The mouse-virulence *E. coli* carrying the Vi antigen, other than the classical strain 5396/38, might well be of value.] *H. J. Bensted*

EGAMI, F., HAYASE, Y. & TANIGUCHI, S. Tentative d'induction de la nitrate-réductase chez un mutant d'*Escherichia coli* auxotrophe pour l'hémine. **[Attempts at Induction of Nitrate-Reductase in a Mutant of *E. coli*, Auxotrophic for Hemin]** *Ann. Inst. Pasteur.* 1960, Mar., v. 98, No. 3, 429–38, 2 figs.

The English summary appended to the paper is as follows:—

"1. H_7 mutants of *E. coli*, auxotrophic for hemin, in aerobic or anaerobic cultures, in presence or in the absence of hemin, never possess nitrate-reductase or formic dehydrogenase.

"2. Particles isolated from H_7 cells in aerobic cultures in presence of hemin or nitrates, contain cytochrome b_1.

"3. H_7 cells do not seem to contain any substance able to inhibit nitrate-reductase.

"4. The findings allow to conclude that mutant cells are not capable to form nitrate-reductase, an enzyme responsible for electron transfer from cytochrome b_1 to nitrates. H_7 appear to be genetically unable to induce the formation of nitrate-reductase and formic dehydrogenase."

WHITESIDE, Roberta E. & BAKER, E. E. **The Vi Antigens of the Enterobacteriaceae. III. A Serologic Study of Native and Deacetylated Vi Antigen isolated from** *Paracolobactrum ballerup.* *J. Immunology.* 1960, Feb., v. 84, No. 2, 221–6, 9 figs. [11 refs.]

"1. Using the Ouchterlony technique, a serologic study was made of native and deacetylated Vi antigen prepared from *Paracolobactrum ballerup* and mixtures of the two.

"2. The data presented indicated that the two zones observed in the reaction of native Vi antigen and antibody were due to the presence of both fully acetylated and partially deacetylated antigens in the preparations studied."

JENKIN, C. R. **The Immunological Relationship of a Protein Toxin from** *Vibrio cholerae* **to its 'O' Somatic Antigen.** *Immunology.* Oxford. 1959, Oct., v. 2, No. 4, 363–7.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 594.]

GHOSH, S. N. & MUKERJEE, S. **Studies on the Nature of Ultrasonic Extract of Cholera Vibrio. Part I: Studies on Toxicity and Pathogenicity.** *Ann. Biochem. & Exper. Med.* 1959, July, v. 19, No. 7, 173–80, 1 fig. on pl.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 593.]

AWAD, N. A. **Growth Rates of Normal and** *Brucella*-**infected Experimental Animals; Effect of Ascorbic Acid and Corticotrophin.** *J. Trop. Med. & Hyg.* 1959, Nov. v. 62, No. 11, 262–8, 2 figs. [14 refs.]

The animals chosen for this study were guineapigs and rats; the former are very susceptible to brucella infections whereas rats may be regarded as relatively resistant to infection with this organism. The infection became established in all the test animals by means of a standard technique. At varying periods test animals were killed to determine the establishment of infection and to collect material for serum agglutination tests. There was an effective number of controls in each group of animals and at regular intervals the weights of the test and control animals were recorded and the brucella agglutinin levels of infected animals were estimated on those killed at 3–4 weeks, 7–8 weeks and 11–12 weeks. The changes in body weight were also studied in other groups of normal and infected guineapigs and rats before and after treatment with ascorbic acid and corticotrophin respectively.

The agglutinin-development pattern was similar in the infected guineapigs and rats but generally the rat titres were lower throughout and at the 11–12 week period were beginning to fall off significantly.

The weight curves for the guineapigs showed a lag in the infected group, maximal at about the 8th week, but after this the curve became steeper and close to the curve for the controls. In the case of the rats, however, the picture was quite different: up to the 8th week the curve for the infected rats was significantly steeper than for the controls but after this the mean body weight fell steadily until at the end of the experiment it was not much above the initial figure.

The most notable effect of ascorbic acid was the sharp increase in weight among the normal rats; there was a slight decrease in the mean body weight of normal and infected guineapigs and also infected rats. With corticotrophin the response of normal guineapigs, normal rats and infected guineapigs was a slight increase, but infected rats showed a marked decrease.

[These results are of interest and are generally what might be expected. Guineapigs are susceptible to experimental infections with brucella organisms, but irrespective of the dose or route of inoculation the infection does not cause much constitutional disturbance. As SHEWELL and LONG showed [this *Bulletin*, 1957, v. 32, 295], the guineapig, like man and the rhesus monkey, is resistant to cortisone, whereas the rat, the mouse, the rabbit and the ferret are sensitive to it. Had Awad's experiments included a study of the antibody response, in addition to the body weight increase, under cortisone treatment in his groups of animals there seems to be little doubt that his results would have been fully in accord with those of Shewell and Long.] *H. J. Bensted*

MISRA, J., AGARWALA, S. C. & SHRIVASTAVA, D. L. **Studies in the Enzyme Make-Up of** *Pasteurella pestis.* **Part VII. Deamination of Purine and Pyrimidine Compounds by Virulent and Avirulent Strains.** *Indian J. Med. Res.* 1960, Jan., v. 48, No. 1, 1–7, 2 graphs.

SAITO, S. **Studies on the Dehydrogenase System of** *Bacterium tularense*. **II. Effect of Surface Active Agents on Succinic Dehydrogenase Activity.** *Fukushima J. Med. Sci.* 1959, Mar., v. 6, No. 1, 23–33, 3 figs. [16 refs.] **III. Effect of Activators, Inhibitors, SH Reagents and Metal Chelating Agents on the Succinic Dehydrogenase Activity.** *Ibid.*, 35–44, 3 figs. [25 refs.] **IV. Effect of X Irradiation and Animal Passage.** *Ibid.*, 45–7. [12 refs.]

LINCOLN, R. E. & DEARMON, I. A., Jr. **Homogeneity of Response of Mouse and Guinea Pig Strains to Virulence Tests with** *Bacillus anthracis* **and** *Pasteurella tularensis*. *J. Bacteriology.* 1959, Nov., v. 78, No. 5, 640–50. [14 refs.]

This paper reports the comparison of the virulence of 2 organisms when tested in groups of various inbred strains of mice and guineapigs and groups of these animals which were not inbred. In these experiments 5 inbred mouse strains and 2 inbred guineapig strains were compared with mouse and guineapig strains from the Fort Detrick laboratories, Maryland, which were not inbred. In assessing virulence it would appear, in general, that the graded response test was more satisfactory than the quantal response test. When spores of *Bacillus anthracis* were used as a challenge in mouse virulence tests it was found that more uniform results were obtained with certain pure mouse lines than with other pure lines or indeed non-inbred lines. Results of the same order were obtained in *Pasteurella tularensis* mouse virulence tests. When, however, the guineapig was the test animal, the results showed that the inbred lines gave less uniform records in the graded response tests than those animals from Fort Detrick which did not come from a pure line or inbred stock.

H. J. Bensted

CHADWICK, P. **Rapid Identification of** *Bacillus anthracis* **by Microscopical Observation of Bacteriophage Lysis.** *J. General Microbiol.* 1959, Dec., v. 21, No. 3, 631–4, 6 figs. on pl.

"When young growing filaments or microcolonies of *Bacillus anthracis* were treated with specific bacteriophage, fragmentation of the filaments followed by complete disintegration of the microcolony were visible microscopically within 2–3 hr. Other Bacillus species were unaffected by the phage. This technique is a simple one for accelerating the identification of *Bacillus anthracis*."

SMITH, H. W. **The Bacteriophages of** *Clostridium perfringens*. *J. General Microbiol.* 1959, Dec., v. 21, No. 3, 622–30, 1 fig. [11 refs.]

"A search has been made for phages active on *Clostridium perfringens*, types A, B, C, D, E, and F. Twelve of 49 type A strains, 10 of 31 type B strains, 10 of 26 type C strains and none of either 38 type D, 5 type E or 3 type F strains were lysogenic. The 'temperate' phages obtained from these lysogenic cultures, together with similar phages obtained from crude material, such as sewage, were only active on strains of the same type as the lysogenic culture from which they were isolated; some of them were very host-specific. It was possible to induce partial lysis in lysogenic strains by ultraviolet radiation, nitrogen mustard and mercaptoacetic acid.

"Other phages isolated from crude material resembled the 'virulent' phages of aerobic bacteria. These phages lysed strains belonging to types A, B, C, D, and F.

"Despite a long search for phages that would lyse them, a high proportion of the strains of *Clostridium perfringens* examined remained insusceptible to all the phages isolated. A close relationship between phage susceptibility and colonial morphology was noted. Smooth and rough strains were usually phage susceptible; mucoid strains were usually phage-resistant."

OAKLEY, C. L. & WARRACK, G. Harriet. **The Soluble Antigens of** *Clostridium oedematiens* **Type D (***Cl. haemolyticum***).** *J. Path. & Bact.* 1959, Oct., v. 78, No. 2, 543–51. [16 refs.]

The anaerobe *Clostridium haemolyticum*, isolated from infectious icterohaemoglobinuria of cattle in the United States, has been investigated with a view to defining more clearly its relationship to *Cl. oedematiens*. It is suggested that this organism might most conveniently be classified as *Cl. oedematiens*, type D, since it is very nearly related to the type B organism in its toxin equipment, producing the β, η and θ components which are also recognized in B strains, but lacking the α toxin characteristic of both A and B strains.

J. W. McLeod

KUJUMGIEV, I. Die Leptospirenserotypen in Bulgarien (Gesamtübersicht und eigener Beitrag). [**Serotypes of Leptospires in Bulgaria. General Survey and Personal Studies**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1960, Feb., v. 6, No. 2, 106–10. [27 refs.]

DIAS, V. M. & DA SILVA, N. da P. M. Diferenciação entre *Listeria monocytogenes* e *Erysipelothrix rhusiopathiae* com o clorêto de trifeniltetrazólio. [**Differentiation of** *Listeria monocytogenes* **from** *Erysipelothrix rhusiopathiae* **with Tetrazolium Salts**] *Mem. Inst. Oswaldo Cruz.* 1958, Dec., v. 56, No. 2, 477–87, 14 figs. (5 coloured) on 2 pls. English summary.

Attention is drawn to the value of media containing salts of 2-3-5-triphenyltetrazolium chloride for the differentiation of *Listeria monocytogenes* and *Erysipelothrix rhusiopathiae*. *Listeria* gives much more active reduction of the tetrazolium salt to formazan with the development of red coloration. The methods of demonstrating this effect both in fluid and solid media are

discussed and the effect of exposure to the dye on bacteria as observed with the electron microscope.

There is no reference to the extensive work of HIRSCH, CATTANEO and MORELLINI on the reduction of these salts by a variety of bacteria and the effect of variations in *p*H on such reduction [this *Bulletin*, 1958, v. 33, 1080; 1959, v. 34, 274, 472, 1043].

J. W. McLeod

TUBYLEWICZ, H. **Studies on the Antigenic Structure of *Listeria monocytogenes*. I. The Chemical Structure of Protein Substances isolated from Eight Strains of *Listeria monocytogenes*.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1960, v. 8, No. 2, 57–60. [10 refs.]

UNITED STATES DEPT. HEALTH, EDUCATION & WELFARE. **Studies on the Serratia Group** [EWING, W. H., DAVIS, B. R. & REAVIS, R. W.]. *CDC Lab. Manual.* 1959, July, 19 pp. [15 refs.] Atlanta: Pub. Health Service, Bureau of State Services, Communicable Disease Center, Georgia.

57 strains of *Serratia* (or *Chromobacterium*) species from the private collection of the late R. S. BREED, from the American Type Culture Collection (ATCC), Washington, and the National Collection of Type Cultures (NCTC), London, together with 83 strains sent to Communicable Disease Center (CDC) for identification [criteria used in selecting these cultures are not stated] were examined by methods used for members of the family Enterobacteriaceae [this *Bulletin*, 1958, v. 33, 507].

Of the 140 cultures examined, 25 (all from culture collections) were excluded since they did not have the characters that the authors decided the *Serratia* group should have. These are: acid and a small volume of gas from glucose, lactose not fermented rapidly, acid from maltose, mannitol, sorbitol, trehalose and salicin; no acid from dulcitol, rhamnose, arabinose or raffinose; variable results from inositol, xylose, adonitol and cellobiose; acid but no gas from glycerol. The following tests are positive: citrate, V-P, nitrate reduction, ammonium-glucose, gelatin liquefaction, KCN, lysine and ornithine decarboxylase. The following are negative: urease, indole, MR, H_2S, phenylalanine, malonate, arginine dihydrolase. Pigmentation is given as a variable character.

Serological analysis produced 9 "O" groups and 13 H antigens; several "O" antigens were related to "O" antigens of *Aerobacter cloacae*, *A. aerogenes*, and *Hafnia alvei*.

[It is passing strange that of 57 strains labelled *Serratia* by other workers, no fewer than 25 were rejected as not belonging to the group. On the other hand, 83 apparently unselected strains sent to CDC for identification fell into the *Serratia* group of these authors, and only 25% of these were pigmented.

The authors do not say how they would classify the 25 pigmented strains labelled by them "Not *Serratia*".]

S. T. Cowan

RICKETTSIAE

ROGER, F. & ROGER, A. Influence du *p*H et de la concentration saline sur la dispersion de *Rickettsia burneti*. [**Influence of *p*H and Salt Concentration on the Dispersion of *Rickettsia burneti***] *Ann. Inst. Pasteur.* 1960, Jan., v. 98, No. 1, 153–6. [10 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 465.]

ZDRODOVSKII, P. F. & GOLINEVICH, E. M. **The Immunogenic Properties of *Rickettsia prowazeki* Strain E.** *Problems of Virology.* London. 1958, v. 3, Nos. 5/6, 284–8. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 462.]

LIGANOVA, Z. A. **A study of the Rickettsiocidal and Insecticidal Properties of Hexylresorcinol.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 2, 165–8. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 576.]

CARVALHO DE SOUZA, J. R., FRANCO, A. P. & PINTO, M. R. Variation de phase antigénique de la *Coxiella burneti* dans des cultures de tissus. [**Variation of Antigenic Phase of *Rickettsia burneti* in Tissue Culture**] *C.R. Soc. Biol.* 1959, v. 153, No. 10, 1673–6.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 579.]

STOENNER, H. G. & LACKMAN, D. B. **The Biologic Properties of *Coxiella burneti* isolated from Rodents collected in Utah.** *Amer. J. Hyg.* 1960, Jan., v. 71, No. 1, 45–51. [13 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 580.]

KORDOVÁ, N. & REHÁCEK, J. **Experimental Infection of Ticks *in vivo* and their Organs *in vitro* with Filterable Particles of *Coxiella burneti*.** *Acta Virologica.* Prague. 1959, Oct., v. 3, No. 4, 201–9, 6 figs. on 3 pls. [20 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 580.]

KORDOVÁ, N. **Study of Antigenicity and Immunogenicity of Filterable Particles of** *Coxiella burneti*. *Acta Virologica.* Prague. 1960, Jan., v. 4, No. 1, 56–62. [15 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 580.]

ROSENBERG, M. & KORDOVÁ, N. **Study of Intracellular Forms of** *Coxiella burneti* **in the Electron Microscope.** *Acta Virologica.* Prague. 1960, Jan., v. 4, No. 1, 52–5, 6 figs. on 3 pls. [19 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 579.]

BACTERIOPHAGES

KOZLOFF, L. M. & LUTE, M. **Calcium Content of Bacteriophage T2.** *Biochim. et Biophys. Acta.* 1960, Jan. 29, v. 37, No. 3, 420–24. [12 refs.]

COCITO, C. & HERSHEY, A. D. **Transfer of DNA-Glucose from Parental to Offspring Phage T2.** *Biochim. et Biophys. Acta.* 1960, Jan. 29, v. 37, No. 3, 543–4.

WEIGLE, J., MESELSON, M. & PAIGEN, K. **Density Alterations associated with Transducing Ability in the Bacteriophage Lambda.** *J. Molecular Biol.* London. 1959, Dec., v. 1, Nos. 4/5, 379–86, 3 figs. & 3 pls. [11 refs.]

TERADA, M., KONDO, I., KUROSAKA, K. & ENOMOTO, Y. **Phage Inactivating Agent closely related with** *Salmonella* **O (XII) Antigen.** *Japanese J. Microbiol.* 1959, Apr., v. 3, No. 2, 145–57, 2 figs. [11 refs.]

2 mutants of a phage Krh derived from *Salmonella sendai* formed pinhole plaques on the indicator *Salm. gallinarum* (Sg) but normal sized plaques on a strain resistant to phage z (Sg/z). The mutants adsorbed to the indicator Sg/z very slowly. On mixture with strain Sg the drop in free phage appeared to suggest much faster adsorption to this strain, but this was not confirmed by plaque counts from the infected host cells. Instead, it was found that phage was being inactivated by the bacterial culture itself, even after filtration or heating to 100°C. Somatic extracts of Sg inactivated the phage and inactivation was prevented by Sg antiserum.

Experiments with other strains of salmonella of Group D, and of other groups, and with absorbed antisera, indicated that the inactivating agent was closely related to the O antigen XII. However, filtrates of Group B salmonella which possess antigen XXVII as well as antigen XII did not inactivate the phage. It is not clear which of the XII antigens was concerned or whether another factor was required to act with it. The authors think that the antigen may constitute or be associated with the phage receptors, and that antigen released from the cell blocks the phage tail, so reducing the efficiency of plating and the plaque size. That ordinary plaques are still formed on Sg/z they presume to be related to the fact that the strain had spontaneously become rough. *Janice Taverne*

VIRUSES

The order in this section is:—**General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.**

LWOFF, A., ANDERSON, T. F. & JACOB, F. Remarques sur les caractéristiques de la particule virale infectieuse. [**Remarks on the Characteristics of the Infectious Virus Particle**] *Ann. Inst. Pasteur.* 1959, Sept., v. 97, No. 3, 281–9. [17 refs.]

The structure of the virus particle is discussed, and a new terminology is proposed to describe its constituent parts. The particle itself is termed the *virion*; it consists of an envelope of protein, the *capsid*, made up of subunits or *capsomeres*, the whole enclosing the genetic material. *D. J. Bauer*

SWARTZ, M. N. & LITTLEFIELD, J. W. **Biochemistry of Viral Infection.** *New England J. of Med.* 1960, Feb. 11 & 18, v. 262, Nos. 6 & 7, 287–95; 342–51, 6 figs. [152 refs.]

"In this review we have tried to summarize current ideas about the mechanism by which bacterial, plant and animal viruses attach to, penetrate, multiply in and are liberated from host cells. The nucleic acids find a central role in the over-all infectious process, and we have emphasized the details of the synthesis of DNA and thoughts on how its structure controls the

structure of related proteins. It has been demonstrated that the impact of a virulent virus on the host's economy can be a consequence of the usurpation of the latter's biosynthetic machinery for the production, almost exclusively, of viral progeny. Although various individualized features, depending on the nature of the host cell, may be required for attachment or penetration, they serve only one purpose—that is, to ensure the intracellular delivery of the 'infectious' component, the nucleic acid. Although, in most cases of viral infection, the information contained in the nucleic acids injected leads as one end result to the death of the host cell, it bears re-emphasis that in certain circumstances, although only so far with bacteriophage, the injection of DNA leads to heritable changes in the host cell not inconsistent with continued growth and division."

FRANKLIN, R. M. & WECKER, E. **Inactivation of some Animal Viruses by Hydroxylamine and the Structure of Ribonucleic Acid.** *Nature.* 1959, Aug. 1, v. 184, 343–5. [19 refs.]

BISHOP, L. W. J., SMITH, M. K. & BEALE, A. J. **An Apparatus for Producing Trypsinized Monkey Kidney Cell Suspensions.** [Correspondence.] *Virology.* New York. 1960, Feb., v. 10, No. 2, 280–83, 2 figs.

HAHON, N. & WILSON, B. J. **Pathogenesis of Variola in *Macaca irus* Monkeys.** *Amer. J. Hyg.* 1960, Jan., v. 71, No. 1, 69–80, 3 figs. [25 refs.]

Monkeys were exposed to aerosols of variola virus adapted to chick embryos. The resulting mild disease manifested itself after an incubation period of about 6 days and lasted for 4 to 7 days. Animals were killed daily during 3 experiments and the virus content of tissues was assayed. Increasing amounts of virus were found in the respiratory tract, especially the lungs. Viraemia was transient and was found towards the end of the incubation period and after the peak of the disease. Virus was found at some time or other in almost all the organs or tissues which were investigated: pancreas, gall bladder, testis, eye and heart are recorded as negative on test. Histological study of respiratory organs and tissues was unrevealing. Although the lungs appeared to be the main site of primary infection and virus multiplication, both control and experimental animals had a pneumonitis and there were no specific features in the histology of lungs from experimental animals.

[The natural history of virus increase in the respiratory tract of monkeys may have a bearing on the spread of smallpox in man despite the dissimilarities of the incubation period and severity of disease in the two hosts. The suggestion that monkeys may act as a natural reservoir of variola virus is mere supposition.]

Colin Kaplan

MCCREA, J. F. & O'LOUGHLIN, Jean. **Effect of Concentrated Urea Solutions on the Infectivity and Haemagglutinin of Vaccinia Virus.** [Correspondence.] *Nature.* 1959, Nov. 7, v. 184, Suppl. No. 19, 1497–8, 1 fig.

Vaccinia virus suspended in or diluted into 8 M urea rapidly loses its infectivity. Vaccinia haemagglutinin, on the other hand, is stable in 8 M urea even when heated at 70°C. for 2 hours, compared with control preparations in phosphate buffer which lose activity rapidly during the first 45 minutes of heating. [Vaccinia haemagglutinin is generally regarded as being heat stable. The results obtained by these authors may be due to a strain difference not so far reported.]

Colin Kaplan

WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. NO. 180. **Requirements for Biological Substances. 5. Requirements for Smallpox Vaccine. Report of a Study Group. Geneva, 3–8 November 1958.** 24 pp. [Refs. in footnotes.] 1959. Geneva: Palais des Nations. [Sales agent for U. K., H.M. Stationery Office.] [1s. 9d.; $0.30; Sw.fr. 1.–.]

This report cannot be readily summarized. As it is the first attempt at internationally agreed minimal requirements for smallpox vaccine it should be studied by all who are responsible for the preparation of smallpox vaccines. *Colin Kaplan*

CRANDELL, R. A. **Multiplication and Cytopathogenicity of Herpes Simplex Virus in Cultures of Feline Renal Cells.** *Proc. Soc. Exper. Biol. & Med.* 1959, Nov., v. 102, No. 2, 508–11, 6 figs. [17 refs.]

HOGGAN, M. D. & ROIZMAN, B. **The Effect of the Temperature of Incubation on the Formation and Release of Herpes Simplex Virus in Infected FL Cells.** *Virology.* New York. 1959, Aug., v. 8, No. 4, 508–24, 7 figs. [11 refs.]

Cultures of the FL strain of human amnion cells were exposed to the NT strain of herpes virus in a multiplicity of 35–75, which was sufficient to ensure that 90% of the cells became infected under the experimental conditions; the cultures were then washed and incubated at various temperatures, and the formation and release of virus were followed by titrations carried out at intervals after infection. At 37°C. intracellular virus appeared after 9 hours and reached a maximum after 17 hours; extracellular virus appeared after 12 hours and reached a maximum after 27 hours, with a yield of 295 pock-forming units per cell. At 31°C. intracellular virus did not appear until 14 hours and very little extracellular virus was found after 26 hours. The results of experiments carried out at 34° and 39·5°C. are also described. *D. J. Bauer*

HOGGAN, M. D. & ROIZMAN, B. **The Isolation and Properties of a Variant of Herpes Simplex producing Multinucleated Giant Cells in Monolayer Cultures in the Presence of Antibody.** *Amer. J. Hyg.* 1959, Sept., v. 70, No. 2, 208–19, 1 text fig. & 6 figs. on 2 pls. [17 refs.]

A strain of herpes simplex virus growing in FL cell cultures in a medium containing pooled human serum (and consequently herpes antibody) normally produced microplaques. Upon passage, a variant was obtained which caused the formation of syncytial giant cells of 4–5 mm. diameter. The variant produced only macroplaques. It could not be distinguished from the parent strain by neutralization tests or by pock formation on the chick chorio-allantoic membrane. The strains were only distinguishable in FL or HeLa cells growing in the presence of herpes antibody. Neither strain formed plaques in the absence of antibody, presumably because the uncontrolled spread of virus destroyed the culture before micro- or macro-plaques became visible.

The macroplaque variant had been isolated in one culture after 20 passages and was never re-isolated. It is suggested that it is a mutant having more power to spread from cell to cell selected by the conditions of culture. The authors speculate on the bearing of their findings on the problem of recurrent herpes infections in man, which always occur in individuals possessing circulating antibody. *Janice Taverne*

YOSHINO, K., TANIGUCHI, H. & TANIGUCHI, S. **Demonstration of the Eclipse Phase of Herpes Simplex Virus by a New De-Embryonation Technique.** *Virology.* New York. 1960, Jan., v. 10, No. 1, 97–111, 6 figs. [33 refs.]

Experiments designed to demonstrate the eclipse phase of animal viruses have sometimes been criticized on the grounds that small amounts of virus can be detected throughout the period, and these may give rise to the new virus. To overcome this difficulty, the authors used a technique which allows all traces of residual virus to be eliminated from infected cells of the chick chorio-allantoic membrane (CAM).

The contents of 12-day eggs were removed, the empty cavity filled with a mixture of Hanks saline and agar and the CAM dropped so that it was supported by the solidified medium. When the CAM was infected with herpes simplex virus and, after a 2-hour adsorption period, washed, traces of virus (about 3×10^3 PFU per egg, representing 0·22% of the inoculum) could still be recovered after 50 washings. When the infected CAM was treated with herpes antiserum, no virus was detected in subsequent washings but infective virus was still present in the CAM homogenate. However, UV-irradiation of the infected CAM followed by 10 washings resulted in the disappearance of all infective virus for an eclipse phase of 10 hours. At 11 hours both intracellular and extracellular virus appeared, the virus, it seems being released as soon as it was formed.

The authors believe that some residual virus which cannot be washed away sticks to the cell wall non-specifically (perhaps in the crypts described by STOKER *et al.* [this *Bulletin,* 1959, v. 34, 175]) where it is inaccessible to antiserum. This virus does not penetrate the cell wall or give rise to new virus. It can be destroyed by UV-irradiation without affecting the growth curve of specifically adsorbed virus or the titre ultimately reached. *Janice Taverne*

BAUER, D. J. & SHEFFIELD, F. W. **Antiviral Chemotherapeutic Activity of Isatin β-thiosemicarbazone in Mice infected with Rabbit-Pox Virus.** [Correspondence.] *Nature.* 1959, Nov. 7, v. 184, Suppl. No. 19, 1496–7.

Although therapeutically effective against the IHD strain of vaccinia virus in mice [this *Bulletin,* 1955, v. 30, 628], isatin β-thiosemicarbazone is inactive against ectromelia virus infection in mice [*ibid.,* 1957, v. 32, 1091]. Infections with rabbit pox virus, however, were shown to be susceptible to the compound. The pox virus infections seem, therefore, to fall into 2 groups concerning their susceptibility to chemotherapy with isatin β-thiosemicarbazone.

Colin Kaplan

BORECKÝ, L. & ZÁVADA, J., with the technical assistance of L. MAASOVÁ & J. KIANICKOVÁ. **Effect of Anticellular Sera on Infection with Myxoviruses. I. The Effect of Antichorioallantoic Serum.** *Acta Virologica.* Prague. 1960, Mar., v. 4, No. 2, 110–23, 11 figs. (5 on 3 pls.) [17 refs.]

HOTCHIN, J. E., DEIBEL, R. & BENSON, Lois M. **Location of Noncytopathic Myxovirus Plaques by Hemadsorption.** [Correspondence.] *Virology.* New York. 1960, Feb., v. 10, No. 2, 275–80, 6 figs.

Monolayers of chick embryo fibroblasts were infected with varying doses of influenza A (PR8 or Asian strains) and tested for haemadsorption [SHELOKOV *et al.*, this *Bulletin,* 1958, v. 33, 799] after 48 hours' incubation. Discrete foci of haemadsorption could be counted and were roughly proportional to the size of the virus inoculum. Foci were usually "comet" shaped, presumably owing to slow currents within the overlay medium. "Comet" formation could be prevented by the use of low concentrations of agar (0·125% to 0·29%) in the overlay.

It is suggested that this method may be adopted for the infectivity assay of myxoviruses.

H. G. Pereira

FAUCONNIER, B. Modification de la réceptivité des hématies animales et humaines aux agglutinines grippales et ourliennes, après traitement de ces hématies par le formol. [**Modification of Haemagglutinability of Animal and Human Erythrocytes after Treatment with Formalin**] *Ann. Inst. Pasteur.* 1960, Jan., v. 98, No. 1, 107–11, 1 fig.

The haemagglutinating activity of influenza A, A1, A2, B and D, mumps and Newcastle disease viruses

was tested against normal and formalin-treated erythrocytes from man, fowl, mouse, guineapig, ox and horse. Haemagglutination of mouse and guineapig cells at 4°C. was enhanced by formalin treatment, this effect being particularly marked with influenza B virus. Formalin treatment of human and fowl cells caused a similar but less pronounced effect, whereas the results obtained with ox and horse cells were variable and in some cases resulted in impaired agglutinability.

H. G. Pereira

BRAND, G. & SCHMIDT, B. L-Antigen bei Influenzavirusstämmen unterschiedlichen Alters und Adaptationsgrades. [**L-Antigens in Strains of Influenza Virus of Different Ages and Degree of Adaptation**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 1, 20–25, 1 fig.

A further investigation has been made of the soluble complement-fixing L antigen produced by certain strains of influenza virus [this *Bulletin*, 1959, v. 34, 95]. In cross-fixation tests with specific antisera it was shown that L antigen was formed by the Mel, Weiss, Shope and WS strains, but not by 3 lines of the PR8 strain, or by 2 B strains (Lee and B55). PR8 antiserum contained L antibody, which reacted with the heterologous L antigen of an A-prime strain. It is concluded that the formation of L antigen is a characteristic of most strains of type A influenza virus, and is not related to degree of adaptation, the formation of filaments or the laboratory age of the strain.

D. J. Bauer

WIRTH, W. Unspezifische Inhibitoren bei der Typisierung neu-isolierter Influenza-Stämme. [**Unspecific Factors inhibiting the typing of Freshly Isolated Strains of Influenza Viruses**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 3, 299–304. [15 refs.]

The English summary appended to the paper is as follows:—

"Six out of seven freshly isolated strains of A_2 influenza virus showed antigenic relations with one another and with the A/Singapore/1/57/strains, when tested with the cross hemagglutination inhibition test. Five of these strains proved to be highly sensitive to the heat stable β-inhibitor which can be destroyed by trypsin treatment nearly completely. The trypsin concentration necessary for this destruction affects the specific antibody titre too. The influenza virus strains A/Germany/58/57 lost its sensitivity to this inhibiting factor during seventeen consecutive passages in the chick embryo allantois sac."

ALEXANDROVA, G. I. **Peculiarities of Haemagglutination Inhibition Test with Type A2 Influenza Viruses.** *Acta Virologica.* Prague. 1960, Jan., v. 4, No. 1, 1–6.

The poor sensitivity of haemagglutination-inhibition tests performed with non-avid strains of Asian influenza virus was shown to be due to the low stability of antibody-virus complex. Haemagglutinin is readil removed from serum-virus mixtures by fowl red cell but not by human O red cells. Haemagglutination inhibition titres were markedly increased by prolongin incubation of serum-virus mixtures before addition o red cells.

Haemagglutination-inhibition tests with Asian influ enza virus can be improved by: (a) use of non-avi virus strains; (b) interaction of serum-virus mixture fo 14–16 hours at 4°C. before addition of red cells an (c) use of human O red cells. *H. G. Pereira*

JANDÁSEK, L. & VOLÁKOVÁ, N., with the technical assistance of V. DOLEZELOVÁ & M. SVOBODOVÁ. **Som Properties of the Haemagglutination Inhibito of Type A2 Influenza Viruses contained in th Serum of Normal Guinea Pigs.** *Acta Virologica* Prague. 1960, Jan., v. 4, No. 1, 7–16, 4 figs. [1 refs.]

Asian influenza strains showed varying sensitivity t normal guineapig serum inhibitors. Of 6 strain investigated, one was entirely insensitive, 2 showed sudden change from sensitivity to insensitivity and were consistently sensitive. Heating and acid treat ment (*p*H 2·0) of normal guineapig serum increased it haemagglutination-inhibiting activity. Alkali treatmen (*p*H 10) caused a less marked increase in activity Inhibition was greatly reduced but not completel abolished by serum digestion with trypsin. Heating c sensitive strains at 56°C. increased their sensitivity t inhibitor. Haemagglutination-inhibition titres wer increased by prolonging serum-virus contact befor addition of red cells. *H. G. Pereira*

ATHANASIU, P., PETRESCO, A., GRUIA, M. & SĂRĂTEANO, D. Modifications biologiques subie par une souche de virus grippal cultivée su des souris vaccinées contre la rage. [**Biologica Modifications in a Strain of Influenza Virus i Mice Vaccinated against Rabies**] *Giorn. d Microbiol.* Naples. 1959, Apr.–June, v. 7, No. 105–11, 1 fig.

ABINANTI, F. R., BYRNE, R. J., WATSON, R. L., POELM L. J., LUCAS, F. R. & HUEBNER, R. J. **Observation on Infections of Cattle with Myxovirus Para Influenza 3.** *Amer. J. Hyg.* 1960, Jan., v. 71, N 1, 52–8. [10 refs.]

A virus identified as Myxovirus parainfluenza (type 1 haemadsorption virus) was isolated from nas secretions or lung tissues of 15 calves or older cattl Most animals were suffering from upper respirato infections diagnosed as shipping fever, usually occu ring in outbreaks but occasionally also as isolat cases. 3 strains were isolated from nasal secretion of apparently normal calves. The role played by t virus under study in the aetiology of shipping fev was confirmed by serological investigations.

Comparative aspects of human and cattle infections by para-influenza 3 virus are discussed and the possibility of transmission of disease from human beings to animals or *vice versa* is considered.

[See also this *Bulletin*, 1960, v. 35, 90.]

H. G. Pereira

CULVER, J. O., LENNETTE, E. H., NAVARRE, G. & KEMPE, C. H. **The Response to Influenza Vaccines as determined by Levels of Complement-Fixing Antibody in the Acute-Phase Sera of Patients with Respiratory Disease.** *J. Immunology.* 1960, Jan., v. 84, No. 1, 98–105, 3 figs.

Antibody response following the administration of formalin-killed influenza A-prime and B vaccines was studied in military recruits. Acute sera from recruits admitted to hospital with respiratory illness were tested by complement-fixation against influenza A-prime and B viral antigens. Evidence is presented showing that antibody titres found in sera collected within the first 4 days of illness were due to previous antigenic stimulus. Antibody responses to a vaccine containing equal amounts of 2 A-prime strains at a total concentration of 700 chick cell agglutination units per ml. appeared at 7 to 8 days after vaccination, reached a peak at 9 to 10 days and persisted for 1 month but was barely detectable, if at all, 2 months later. The response to the same dose of an influenza B vaccine was higher and persisted longer. *H. G. Pereira*

ROSEN, L. **Hemagglutination-Inhibition Technique for Typing Adenoviruses.** *Amer. J. Hyg.* 1960, Jan., v. 71, No. 1, 120–28, 1 fig. [13 refs.]

Adenovirus types were divided into 3 groups according to their ability to agglutinate monkey (rhesus) or rat erythrocytes: (a) a first group consisting of types 3, 7, 11, 14 and 16, which agglutinate only monkey erythrocytes; (b) a second group consisting of types 8, 9, 10, 13, 15 and 17 which agglutinate rat cells completely and occasionally (types 9, 13 and 15) also monkey cells to lower titres; (c) the third group includes types 1, 2, 4, 5 and 6 which agglutinate rat cells incompletely and do not react with monkey cells. Types 12 and 18 failed to agglutinate monkey or rat cells. Cross tests were performed within each group by haemagglutination-inhibition with rabbit antisera and the appropriate erythrocyte suspensions. The homologous were always considerably higher than the heterologous titres but cross reactions were observed between types 7, 11 and 14 in the first group and between types 8 and 9 in the second group.

The haemagglutination-inhibition technique was successfully applied to the typing of 417 adenovirus strains which were identified as known types in all but 46 instances. The latter were classified in 9 apparently new serotypes.

[The detailed description of the typing technique should be read in full by workers interested in this subject.] *H. G. Pereira*

BINN, L. N. & HILLEMAN, M. R. **A Guinea Pig Potency Test for Adenovirus Vaccine.** *J. Immunology.* 1960, Jan., v. 84, No. 1, 20–26, 1 fig. [18 refs.]

The antigenicity of formalin-killed adenovirus vaccines was tested by measuring antibody responses of guineapigs vaccinated with varying doses. Repeated tests on given vaccines gave consistent results and considerable variation was observed among batches from different manufacturers. The authors recommend that a standard vaccine should always be included in potency tests. *H. G. Pereira*

PEREIRA, H. G., ALLISON, A. C. & BALFOUR, Brigid. **Multiplication of Adenovirus Type 5 studied by Infectivity Titrations and by the Fluorescent Antibody Technique.** *Virology.* New York. 1959, Mar., v. 7, No. 3, 300–314, 6 figs. [25 refs.]

In HeLa cells infected under single-cycle conditions with type 5 adenovirus and examined by the indirect fluorescent antibody technique at intervals after infection, virus antigen was first detected after 12 hours in the form of 6–10 intranuclear granules situated near the nuclear membrane. After 16–20 hours fluorescence also appeared in the cytoplasm; by this time the nuclear fluorescence had become confluent. In infectivity studies of homogenized cells a fall in titre of intracellular virus was observed at 8 hours, followed by a rise which continued to attain a maximum value after 32 hours. The infectivity titre of the culture fluid also rose, but was at all times lower than that of the homogenized cells. The results indicated that virus multiplication begins after an eclipse phase of 8 hours, and is followed by release of virus 8 hours later. The average yield of virus per cell was $10^{3 \cdot 7}$ TCD50, or about $10^{4 \cdot 7}$ virus particles [see this *Bulletin*, 1959, v. 34, 503]. *D. J. Bauer*

JOHNSON, K. M., CHANOCK, R. M., COOK, M. Katherine & HUEBNER, R. J., with the technical assistance of Lotta CHI, Doris WONG & H. C. TURNER. **Studies of a New Human Hemadsorption Virus. I. Isolation, Properties and Characterization.** *Amer. J. Hyg.* 1960, Jan., v. 71, No. 1, 81–92, 1 fig. [17 refs.]

An apparently new member of the myxovirus group was isolated from a young adult patient with afebrile upper respiratory illness and from 30 infants observed in an orphanage nursery. The virus, provisionally named M-25 virus, was isolated in monkey kidney cultures where it was detected by the haemadsorption technique. After serial propagation in monkey kidney cultures it caused a cytopathic effect characterized by the appearance of scattered small granular round cells and small eosinophilic cytoplasmic inclusions. The virus could also be propagated in cultures of human, hamster and bovine embryo kidney tissues but not in HeLa, monkey heart, rabbit kidney or human liver (Chang) cells. It was non-pathogenic for adult mice

inoculated intraperitoneally, intranasally and intracerebrally or to newborn mice inoculated intracerebrally and intranasally. Adult or newborn hamsters similarly inoculated showed no signs of illness but virus recovery from lung suspension of inoculated animals suggested that virus multiplication may have taken place in this host. Guineapigs also appeared to be susceptible to inapparent infection. Repeated attempts were made to propagate the virus in embryonated eggs and the results indicate poor, if any, virus multiplication. The M-25 virus was ether-sensitive and relatively thermolabile. Filtration experiments indicated a size between 192 and 248 mμ.

Haemadsorption could be detected in monkey kidney cultures infected with M-25 virus giving, at the fourth passage level, strong reactions with monkey and guineapig cells, weaker reactions with human O cells and no reaction with fowl or rat cells. With further tissue culture passages strong haemadsorption with fowl red cells was obtained. Treatment of red cells by *Vibrio cholerae* receptor destroying enzyme abolished their capacity to be adsorbed. Fluids from infected cultures had low haemagglutinating activity demonstrable at 4°C. or at room temperature. Agglutinated cells were dispersed when transferred to 37°C. and reagglutinated by cooling.

No antigenic relationship was found between M-25 virus and vaccinia, herpes simplex and reovirus types 1, 2 and 3. Complement-fixation tests done with guineapig antisera failed to show cross-reactions between M-25 and other members of the Myxovirus group including influenza A2, B and C, para-influenza 1, 2 and 3, mumps, Newcastle disease virus and a simian haemadsorption virus. In similar tests performed with human convalescent sera the M-25 virus was shown to be antigenically unrelated to influenza A1, A2, B and C or to para-influenza 1, 2 and 3. A patient infected with M-25 virus and 1 of 10 children from whom the same virus was isolated showed, however, small antibody rises against para-influenza 3 virus. Rises in complement-fixing antibodies for M-25 virus were detected in paired sera from adults, but not from children, infected with mumps virus.

H. G. Pereira

TYRRELL, D. A. J.; BYNOE, M. L.; HITCHCOCK, G.; PEREIRA, H. G.; ANDREWES, C. H.; PARSONS, R. **Some Virus Isolations from Common Colds. I. Experiments employing Human Volunteers** [TYRRELL, BYNOE, HITCHCOCK, PEREIRA & ANDREWES]. *Lancet.* 1960, Jan. 30, 235–7. [12 refs.] **II. Virus Interference in Tissue Cultures** [HITCHCOCK & TYRRELL]. *Ibid.*, 237–9, 1 fig. **III. Cytopathic Effects in Tissue Cultures** [TYRRELL & PARSONS]. *Ibid.*, 239–42, 3 figs.

I. These 3 papers describe the isolation of viruses from patients with common colds, their propagation in tissue culture and methods for their *in vitro* recognition without recourse to human-volunteer experiments. The first paper describes the results of human-volunteer experiments. In 1953 ANDREWES *et al.* [this *Bulletin*, 1954, v. 29, 780] described the propagation of a strain of common cold virus DC in human embryo lung cultures. Despite many attempts no success was achieved beyond the 10th passage of DC virus. Organ culture was attempted but gave irregular results after 1 passage and no colds with higher passages. Trypsinized human embryo kidney cultures grown in medium 199 were found to be much more successful for propagating viruses from adult patients with colds. 3 viruses, PK, HGP and FEB, were successfully propagated through 8 passages. The results of the human-volunteer experiments suggested that incubating the cultures at 33°C. rather than 36°C. and harvesting them at 4 days rather than 2 or 6 days produced best results.

The specificity of the human-volunteer results were controlled by inoculating (a) medium alone, (b) broth saline that had been passed in human embryo kidney cultures in parallel with the nasal washings, (c) nasal washings passed in (i) tubes containing medium only or (ii) calf kidney cells. The danger of an accidental pick-up of virus is illustrated in Table III where it is stated that the results on 5 volunteers given control material were vitiated because of the discovery of ECHO 11 virus in it.

II. In the second paper it is shown that human embryo kidney cultures infected with agents from common colds yielded less haemagglutinin than control cultures when challenged with Sendai or ECHO 11 viruses. Interference was detected at 4 or 5 days after the addition of a cold virus but not at 2 or 8 days. The best results were obtained by assaying the haemagglutinin produced by the challenge virus 2 to 3 days after inoculation of 0·2 HA units. The difference between the $\log_2$ geometric mean HA titres of 5–10 test cultures and a similar number of control cultures was called the interference index. With this technique it was found that 2 out of 4 nasal washings from adults with colds yielded an interfering agent in the acute stage but not the convalescent stage. Similarly a pool of washings from volunteers infected with HGP virus had an interfering agent in the acute but not the convalescent stage. On the other hand volunteers given DC material yielded no interfering agent. The presence of other viruses in the serially propagated cold virus materials was tested by haemagglutination and haemadsorption with human, chicken, ox, mouse and guineapig cells. Guineapigs, rabbits and weanling (and suckling) mice were unaffected by virus inoculation. No interference was obtained in calf or monkey kidney or in human thyroid cells. The addition of 0·1% glucose and 0·2% bovine plasma albumin appeared to increase the growth of the cold viruses judged by interference.

III. The third paper describes the observation of cytopathic effects of 3 of the agents isolated from common colds on human embryo kidney cells grown in medium 199 with low levels of sodium bicarbonate (originally 0·09% instead of 0·16%). The cytopathic effects were similar to those of a slowly growing member of the enterovirus family. 2 of the strains, HGP and PK, also produced cytopathic effects in monkey kidney cells. Best results were obtained with lightly grown second generation cells. It has been found that lactalbumin hydrolysate medium with 0·03% bicarbonate and calf serum up to 4% gave satisfactory result

at 33°C. The observation of cytopathic effects was independently confirmed in 2 other laboratories. Cytopathic effects and interference were obtained with all 3 strains in human embryo kidney cultures. Although 2 strains caused cytopathic effects in monkey kidney cells neither produced interference with Sendai or ECHO 11 in these cells. The properties of the viruses detected by interference, by cytopathic effect and in human volunteers were the same. Thus the HGP strain was resistant to ether, destroyed by 56°C. in 30 minutes (not tested in volunteers), destroyed by *p*H 2 and passed a 290 mμ gradocol membrane filter (not tested in volunteers). It was also inhibited by human gamma globulin in tests in volunteers, and unaffected by Arcton 63 in tests for cytopathic effects.

[This important work may be the first sign of the long awaited break-through in the study of common colds in adults. The authors are careful to point out that the Salisbury viruses are not yet established as common cold viruses. They should, however, soon be able to establish whether they do produce colds regularly in volunteers and can be frequently isolated from colds. The means are also available for determining their antigenic relationships to each other and to other viruses.] *A. J. Beale*

MAURIN, J., CARRÉ, M. C. & VIRAT, J. Etude des virus entériques de l'homme. Isolement, identification et recherches sérologiques en 1958. [**Studies on Enteroviruses in Man. Isolation, Identification and Serological Studies, 1958**] *Ann. Inst. Pasteur.* 1960, Feb., v. 98, No. 2, 211–23. [11 refs.]

This paper records the total isolations of enteroviruses in monkey kidney cells at the Pasteur Institute in 1958. The patients were mainly suspected of having paralytic poliomyelitis or meningitis. There was less poliomyelitis in France in 1958 than in 1957 and there was a change in type distribution. Thus in 1957 nearly 90% of the isolations were type 1 and only 4·3% type 3 whereas in 1958 the figures were type 1, 71·4%, type 2, 6·5% and type 3, 22·1%. During 1957 and 1958, 85 other enteroviruses were isolated: 22 Coxsackie B, 1 each ECHO types 1 and 9, 4 ECHO types 14, and 57 as yet unidentified. A few preliminary results obtained with the complement-fixation test with poliovirus antigens are presented but the diagnostic value of this test remains to be determined. *A. J. Beale*

ŽEMLA, J. & PESEK, J. **Titration of Polioviruses in Human Amnion Cells, using the Colour Test on Plastic Panels.** *Acta Virologica.* Prague. 1959, Oct., v. 3, No. 4, 253–7. [22 refs.]

The authors describe a modified method of colour test titrations [this *Bulletin*, 1955, v. 30, 184; 1956, v. 31, 958] for poliovirus by using a continuous line of human amnion cells derived by MAYER *et al.* (*Acta Virologica*, Suppl., 1959, v. 3, 51). The titres, especially for type 1, were lower in early passages in the human amnion cells than they were in later ones as the strains became adapted to the new cells. The titres in HeLa cells and human amnion cells were roughly the same by the colour method and by the observation of cytopathic effects. *A. J. Beale*

YANG, Czau-Siung, CHOU, Chi-Tao, LAI, Jeuy-Shin & SHIAO, Liu-Ching. **Studies on Poliovirus in Tissue Culture. I. Isolation of Poliovirus with Taiwan Monkey Kidney Cells (1957–1958).** *J. Formosan Med. Ass.* 1959, Sept. 28, v. 58, No. 9, 540–48, 7 figs. on 2 pls. [12 refs.]

"1. Taiwan monkey kidney cells grown in a medium which consists of 0·5% lactalbumin enzymatic hydrolysate and 6% buffalo serum in Earle's balanced salt solution were used for the isolation and typing of polioviruses.

"2. Of 160 species tested (121 from 103 polio patients, 20 from 17 non-polio patients, and 19 from 19 family members of the patients), 49 strains of poliovirus and 7 other cytopathogenic agents were isolated. The type distribution of polioviruses was 28 Type 1, 17 Type 2 and 4 Type 3. One Type 1 strain was isolated from the throat swab specimen of a polio patient.

"3. About 57% (7 of 12) of the polioviruses isolated in 1957 were of Type 2 and 62% (23 of 37) of the virus in 1958 belonged to Type 1.

"4. Examination of multiple rectal swab specimens favors the detection of polioviruses."

LWOFF, A. & LWOFF, Marguerite, with the technical collaboration of Evelyne RITZ & Marie C. MAIGNÉ. Sur les facteurs du développement viral et leur rôle dans l'évolution de l'infection. [**The Factors of Viral Development and their Role in the Evolution of Infection**] *Ann. Inst. Pasteur.* 1960, Feb., v. 98, No. 2, 173–203, 11 figs. [44 refs.]

This important paper gives the experimental details and full discussion of the authors' work on the importance of the non-specific factors, temperature and *p*H, on the growth of viruses *in vitro* and their probable role *in vivo*. This work has been summarized and discussed by LWOFF in English (*Bact. Reviews*, 1959, v. 23, 109).

The development of type 1 polioviruses in KB cells was studied at different temperatures. It was found that the pattern of development at different temperatures varied greatly from strain to strain. In general the yield of virus fell with rising temperature, but very much less for neurovirulent strains than for attenuated strains. The attenuated type 1 vaccine strains of Sabin (LSc 2 ab) and Koprowski (Chat) gave closely similar yields at temperatures from 35°C. to 40°C. Both more and less temperature-sensitive variants [temperature-sensitive in the sense that the yield was less in cells maintained at 40°C.] of Sabin's strain and of the Brunenders strain [this is used as the type 1 component of British poliovaccine] were selected. The vaccine strains were temperature-sensitive and a strain of Brunenders obtained by 8

passages at 25°C. was not neurovirulent for monkeys, whereas the less temperature-sensitive strains proved to be neurovirulent for monkeys. The temperature-sensitive step occurred late in the course of virus development.

The effect of *p*H on virus development was also studied and it was found that a *p*H of less than 6·9 virus development was considerably delayed. Since low *p*H and high temperature are unfavourable to virus development the fever and low *p*H of inflammatory exudates are considered valuable non-specific defence mechanisms *in vivo*. Examples of these effects from the literature are cited. It follows that strains of virus capable of surmounting these defences will be virulent.

[This is a most interesting paper. Readers wishing to read a discussion of the main points in English should see Lwoff *loc. cit.* If the full technical details are required then this paper should be consulted.]

A. J. Beale

COID, C. R. & BESWICK, T. S. L. **Production of Viraemia in Cortisone-Treated Monkeys with the Attenuated Brunenders Strain of Type-1 Poliovirus.** *Lancet.* 1960, Feb. 20, 414–15.

In England the partially attenuated Brunenders strain is used as the type 1 component of killed polio-vaccine. The authors point out that the requirements for the monkey safety of poliovaccine have been worked out with virulent strains of poliovirus. With a total dose of between 3 and 140 TCD50 of Brunenders virus diluted either in medium 199 or in vaccine, 68 monkeys were inoculated, intrathalamically, intraspinally and intramuscularly. They were given cortisone intramuscularly 2 days before and on alternate days for 16 days after inoculation. It was found that poliovirus detection was improved by combined virus isolation attempts from the serum and histological examination of the central nervous system. Thus 33 animals were found to be infected, 13 detected by both methods, 12 by viraemia only and 8 by central nervous system lesions only [no virus isolations were attempted from the central nervous system]. Virus isolations were attempted between 3 and 18 days and the first isolation of virus occurred almost uniformly throughout the sampling period. Thus 6 of the isolations were first obtained after 15–18 days. Virus was detected in 16 out of 27 animals given virus in medium 199 and in 17 out of 41 given virus in vaccine.

A. J. Beale

YOSHIOKA, I., RIORDAN, J. T. & HORSTMANN, Dorothy M. **Thermal Sensitivity of Polioviruses isolated during Oral Vaccine Field Trial: Comparison with Monkey Neurovirulence.** *Proc. Soc. Exper. Biol. & Med.* 1959, Nov., v. 102, No. 2, 342–7, 1 fig. [10 refs.]

The value of the T marker in assessing the neurovirulence of strains of poliovirus isolated during a field trial of SABIN's strains of attenuated poliovaccine was studied. Virulent strains of poliovirus grow readily at 39° or 40°C. whereas attenuated strains do not (see LWOFF and LWOFF, *C.R. Acad. Sci.*, 1959, v. 248, 154). Strains were grown at 35°C., 37°C. and 39°C. and the titres were expressed as the logarithms of the ratio to the titre at 37°C. If this was −4·0 or more the strains were designated T, the characteristic of attenuated strains (*i.e.* the titre at 39°C. was 1/10,000 that at 37°C.); if −2·1 to −4·0 intermediate, and if −2·0 or less T +, the characteristic of virulent strains. Second or third monkey kidney passage material was used for the T tests. Tests were also performed for the d marker [VOGT *et al.*, this *Bulletin*, 1958, v. 33, 891] and for neurovirulence by the intracerebral route in monkeys. [This is here called the M marker which is rather unfortunate as ability to grow on the MS line of monkey kidney cells is called the MS marker and may lead to confusion.]

It was found that virulent strains type 1 Mahoney, type 2 MEF 1 and type 3 Leon were T + and M + whereas Sabin's attenuated strains (LSc, YSK and Leon KP_{34}) were T − and M −. The Mahoney strain was d + and LSc d −.

Strains of virus isolated during a trial of Sabin's type 1 virus in a village community near Phoenix, Arizona [HORTSMANN *et al.*, *ibid.*, 1960, v. 35, 274] were studied for all these genetic markers. Strains isolated from 2 individuals who were given type 1 virus by mouth were T − d − M −. One child excreted a T + d + M + strain at 14 days. 2 earlier isolates from this child had been T − d − but each had caused lesions in 1 of 2 monkeys inoculated intracerebrally. A similar pattern was observed in a strain isolated from a privy used by a family given vaccine virus by mouth. 15 viruses were isolated from flies during the trial. One was T − M − the rest were I or T + and M +. The correlation between T and M markers was better than between d and M. It is concluded that the T marker is a useful guide to the degree of virulence of strains and noted that even more clear-cut results might have been obtained if 40°C. rather than 39°C. had been used. It was hoped that these 3 markers could be used to distinguish the vaccine strains from wild strains, but it was found that in communities with many naturally circulating polioviruses of varying virulence this was a very complex matter.

[The exact manner of performing a T test may be of great importance. The methods of Lwoff, Sabin and the present authors differ substantially. Sabin's method consists of performing parallel titrations in tubes at 36° and 40°C. and reading results after 14 days. A 10^5 to 10^6 lower titre is found at 40°C. compared with 36°C. for attenuated strains.

The d, T and M markers do not seem to be adequate for identifying vaccine strains in the community, a requirement for attenuated vaccines suggested by DICK and DANE [this *Bulletin*, 1957, v. 32, 311]. It may be that the serological character K [MCBRIDE, *ibid.*, 1959, v. 34, 833] will prove to be a suitable character for this purpose since it appears to be much more stable than other characters so far delineated.]

A. J. Beale

THOMSSEN, R., DOSTAL, V., HAAS, R. & RUSCHMANN, E. Untersuchungen zur thermischen Resistenz von Polioviren. [**The Thermal Resistance of Poliovirus**] *Arch. f.d. gesamte Virusforschung.* 1960, v. 9, No. 5, 571–81, 5 figs. [14 refs.]

The English summary appended to the paper is as follows:—

"Studies on the thermal inactivation of poliomyelitis virus type 1 (Mahoney), prepared in monolayer tissue cultures of trypsinized monkey kidney cells, were made at a temperature of 45°C. Evidence was furnished of the presence in the virus fluid of substances of low molecular weight, which increase the rate of thermal inactivation. These substances could be eliminated by dialysis, whereby thermal resistance became greatly increased. Inhibition of thermal inactivation was possible by addition of chelating agents as EDTA and partly by KCN. Addition of aminoacids had a similar effect. The data pointed to the possible role of metal ions. Therefore we tested the effect of some metal salts. Cr^{+3}-salts increased the rate of thermal inactivation."

WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. NO. 178. **Requirements for Biological Substances. 1. General Requirements for Manufacturing Establishments and Control Laboratories. 2. Requirements for Poliomyelitis Vaccine (Inactivated). Report of a Study Group. Geneva, 2–7 June 1958.** 30 pp. [Refs. in footnotes.] 1959. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [1s. 9d.; $0.30; Sw.fr. 1.–.]

A study group composed of the people most concerned with the control of biological products in most of the countries which make poliovaccine has recommended requirements for the manufacture of poliovaccine. These follow closely the requirements of the United States national control laboratory. They will form a valuable guide to control authorities in countries where the manufacture of poliovaccine may be started in future, embodying as they do the fruits of hard-won experience. At present there is no standard preparation of poliovaccine nor a generally accepted technique for potency testing. Steps are now being taken towards establishing such a standard under the auspices of the WHO Expert Committee on Biological Standardization. *A. J. Beale*

GHENDON, I. Z. & MARCHENKO, A. T. **A Method for the Rapid Determination of Immunogenic Potency of Poliomyelitis Vaccines by Single Vaccination of White Rats.** *Acta Virologica.* Prague. 1959, Oct., v. 3, No. 4, 250–52.

The authors have previously described the use of white rats for testing the potency of poliovaccine [this *Bulletin*, 1959, v. 34, 1194]. Formerly they used 2 doses, now they recommend 1 intraperitoneal dose and bleeding 4 days later. After 1 dose antibodies are said [no experimental details are given] to reach a peak at 4–5 days and thereafter to fall quickly. An antigen extinction test as advocated by GARD is performed with 10 animals at each 10-fold dilution. Sera are tested at a 1/4 dilution in a metabolic inhibition test [*ibid.*, 1956, v. 31, 958]. The results for 20 batches of vaccine are presented in a table. It is concluded that white rats are a satisfactory species for testing the potency of poliovaccine, having the advantage of being very hardy and insusceptible to poliovirus so that a living standard antigen can be used to control the sensitivity of the tests.

A. J. Beale

CABASSO, V. J., JERVIS, G. A., MOYER, A. W., ROCA-GARCIA, M., ORSI, E. V. & COX, H. R. **Cumulative Testing Experience with Consecutive Lots of Oral Poliomyelitis Vaccine.** *Brit. Med. J.* 1960, Feb. 6, 373–87, 6 charts & 3 figs. [16 refs.]

This is a long and detailed account of the methods of preparing and testing living attenuated poliovaccine employed by Lederle Laboratories. A summary of the origin and subsequent history of the 3 strains used is given. These are SM (type 1) MEF 1 (type 2) and Fox P1149 (type 3). The tests required for a living attenuated poliovaccine must ensure (a) the absence of organisms whether harmful or not, other than poliovirus, (b) the continued avirulence of the poliovirus, (c) the antigenic potency of the poliovaccine. Unfortunately only the first of these can be achieved without feeding the virus to man (or perhaps chimpanzees).

Methods used to exclude other organisms were as follows: kidneys from individual monkeys were processed separately and the virus grown for the resulting cultures was tested separately before pooling into larger batches. Virus before testing was filtered through a Hormon D9 asbestos filter. Routine tests for bacteria and fungi were performed at 37°C. and room temperature. Viruses other than poliovirus were tested for with poliovirus immune serum made by inoculating rabbits or chickens with virus grown on HeLa cells. This was done to exclude, so far as is possible, antibodies to simian viruses. The neutralized poliovirus was inoculated in a total volume 2 ml. into monkey kidney cultures and the same volume into HeLa cells in order to detect simian or measles viruses. Subsequently the virus taken from storage at − 20°C. was inoculated into 12 adult mice, 3 litters of newborn mice, 3 rabbits and 3 guineapigs mainly to exclude herpes B virus (Sabin's B virus) central nervous system viruses including Coxsackie and tubercle bacilli.

Finally the vaccine was tested for residual neurovirulence either on harvests from single monkeys or from larger pools. Cynomolgus monkeys were used and inoculations were performed by the intracerebral and intraspinal routes with undiluted virus pools and 10^{-1} and 10^{-2} dilutions. Usually 22 animals were used for each route of inoculation. The results showed that the batches of vaccine made from all 3 strains had a relatively high neurovirulence by the intraspinal route.

Thus the overall paralytic rates were: type 1, 37%, type 2, 38% and type 3, 31% and incidences of histological lesions in the lumbar cord were: type 1, 65%, type 2, 75% and type 3, 75%. The results for intracerebral inoculation showed overall paralytic rates and incidence of histological lesions in the lumbar cord for type 1, 1·5% and 7%, type 2, 4% and 44%, and type 3, 1% and 11%, respectively.

The authors are very critical of the intraspinal test. In their initial tests they scored every monkey regardless of whether there was evidence of placement of the virus in the grey matter of the cord, contending that virus that is incapable of spreading from white to grey matter must be of very low invasiveness. However, they note that the method of inoculation and of scoring lesions introduced by MELNICK *et al.* [this *Bulletin,* 1960, v. 35, 317] gives an even higher percentage of lesions and paralysis with their strains. They believe that this technique may be too traumatic (though Melnick does not agree since he gets no lesions with control materials) and too difficult to reproduce. Thus in tests on one lot of type 3 vaccine, 2 tests with a 20-gauge needle gave paralytic rates of 6% and 57% and with a 27-gauge needle (in the U.S. a 27-gauge needle, used by Melnick, is much finer than a 20-gauge needle and may cause more trauma from the fine jet inoculated) 9 out 10 animals who were given undiluted virus were paralysed. Finally, they believe that the intraspinal test may be unrealistically stringent since each of their strains has now been given without any ill effect to about 500,000 individuals of whom at least 50,000 are estimated to have been without homotypic antibodies. Surely, they say, this is far more impressive evidence of safety than any number of neurovirulence tests involving inoculation of virus actually into the anterior horns of the spinal cords of monkeys. More avirulent strains can be developed but they wonder if these will prove as antigenic in man as their present vaccine strains [COX *et al., ibid.,* 1960, v. 35, 57].

[This is a valuable account but unfortunately the plates showing histological lesions are too small and poorly reproduced to be of any value. The methods of testing are not as stringent as those likely to be imposed in the U.S.A. and U.K. for the licensed manufacture of attenuated poliovaccine. In particular, animals will have to be quarantined, a proportion of the cells (probably 25%) will have to be kept as uninoculated controls for the presence of simian viruses and the fluids will have to be tested for extraneous viruses before filtration.

The argument about measurement of avirulence loses a good deal of its force because (a) more attenuated—and reputedly as effective—strains are available (SABIN's strains); (b) the justification for taking the small risk of feeding strains known to retain some neurovirulence must depend upon circumstances. If no alternative form of vaccination is available and poliomyelitis is severe and epidemic the risk is justified, but otherwise it is not—at least in this reviewer's opinion.

In assessing neurovirulence of vaccine lots it would seem important (a) to test the seed virus or other control material of known "virulence" concurrently; (b) to include a test of invasiveness—since, as Sabin pointed out, a virulent virus must not only attack neurones but also reach them. Also, 1 virulent mutant in a batch of vaccine may well be interfered with in a test involving direct inoculation of many virus particles into the central nervous system, but may reveal itself when administered by a peripheral route, for example intramuscularly.] *A. J. Beale*

GIFFORD, G. E. & BLAKEY, B. R. **Effect of 2,4-Dinitrophenol on Replication of Poliovirus in HeLa Cells.** *Proc. Soc. Exper. Biol. & Med.* 1959, Nov., v. 102, No. 2, 268–71, 2 figs. [15 refs.]

It was found that the yield of HeLa cells infected with type 1 poliovirus was the same in normal cells as in those treated with dinitrophenol at levels stimulating glycolysis. The senior author had previously reported [GIFFORD and SYVERTON, this *Bulletin,* 1958, v. 33, 533] that the yield of poliovirus was unaltered in cells maintained anaerobically although the latent period was prolonged. It was expected since dinitrophenol uncouples aerobic oxidative phosphorylation that it would also cause a prolonged latent period without affecting final yield. However, neither latent period nor yield was affected by non toxic levels of dinitrophenol. *A. J. Beale*

KELLY, Sally M. & SANDERSON, W. W. **The Effect of Chlorine in Water on Enteric Viruses. II. The Effect of Combined Chlorine on Poliomyelitis and Coxsackie Viruses.** *Amer. J. Pub. Health.* 1960, Jan., v. 50, No. 1, 14–20, 5 figs. [14 refs.]

The disinfection of sewage by chlorine depends mainly upon the action of combined chlorine—combined, that is, mainly with nitrogenous organic matter. 2 strains of type 1 poliovirus and Coxsackie B5 were used. It was found that the inactivation was greater at low *p*H than at higher values in the range *p*H 6–10. To a lesser extent the rate of inactivation depended on the virus strain or type. Inactivation at *p*H 8 and 25°–28°C. with 1 p.p.m. combined chlorine was apparently linear. Survivors of combined chlorine inactivation were no more resistant than the original strain. 0·5 p.p.m. with a contact period of 15 minutes is common practice for sewage disinfection. This is inadequate, 9 p.p.m. being required to inactivate enteroviruses in 30 minutes and 6 p.p.m. in 1 hour. At 0·5 p.p.m. more than 7 hours' contact is required.

[See also this *Bulletin,* 1959, v. 34, 295.]

A. J. Beale

DÖMÖK, I. **Studies on the Interaction between Coxsackie and Poliomyelitis Viruses. III. The Course of Resistance to Poliomyelitis Virus induced by Coxsackie B1 Virus in Young Mice.** *Acta Virologica.* Prague. 1959, Oct., v. 3, No. 4, 222–33, 1 fig. [14 refs.]

This interesting paper extends observations on the interference to the Lansing strain of type 2 poliovirus

induced by Coxsackie B1 on inoculation of suckling mice [DÖMÖK, this *Bulletin*, 1957, v. 32, 817; 1958, v. 33, 893]. Prior inoculation, either intracerebrally or subcutaneously, with Coxsackie B1 virus into 9-day-old mice conferred upon the survivors (the Coxsackie B1 virus kills approximately 30–50%) a resistance to subsequent challenge with Lansing strain of type 2 poliovirus intracerebrally. This was expressed as a lower titre of poliovirus and a longer survival time. 21-day-old mice were not protected against poliovirus by Coxsackie B1. The resistance appeared by 5 days and was at a peak till 20 days after inoculation of Coxsackie B1. Thereafter the level of resistance declined slightly but was little changed between the 25th and 60th days. The early effect is ascribed to interference and since the late effect is continuous with the early effect, this too is probably an interference phenomenon.

A. J. Beale

IONESCO-MIHĂIEȘTI, C., SERGIESCO, Dina, BUIMOVICI, Elena, KLEIN, R., ZAMFIRESCO, M. & HORODNICEANU, F. Recherches sur le virus Coxsackie. III. La distribution des types antigéniques de virus (1953–1957). [**Investigations on Coxsackie Virus. III. Distribution of Antigenic Types (1953–1957)**] *Arch. Roumaines Path. Expér. et Microbiol.* 1959, Sept., v. 18, No. 3, 373–83. [29 refs.]

67 strains of Coxsackie virus isolated in Rumania in 1953–57 in suckling mice were typed with antisera prepared in rabbits immunized with the prototype strains. The strains were classified as Group A or B on the basis of histological examination of suckling mice inoculated subcutaneously. Subsequently, the strains were typed first against mixtures of antisera and finally against individual sera, in suckling mice. 55 strains were typed satisfactorily (1 in tissue culture, not mice) A1, 1; A2, 4; A3, 2; A4, 8; A5, 16; A6, 13; A7, 4; A9, 1; A10, 4; B3, 1; B4, 1. A mixture of A5 and A9 and A2 and A5 was found. 1 local A9 strain would grow in monkey kidney cells but not HeLa cells. The Coxsackie B3 strain produced cytopathic effects both in HeLa and monkey kidney cells as did other Coxsackie B strains which were not neutralized by B1-4 antisera.

A. J. Beale

GOULET, N. R., COCHRAN, K. W. & BROWN, G. C. **Differential and Specific Inhibition of ECHO Viruses by Plant Extracts.** *Proc. Soc. Exper. Biol. & Med.* 1960, Jan., v. 103, No. 1, 96–100. [15 refs.]

The authors determined the therapeutic index (ratio of minimal toxic to minimal effective dose) for a variety of plant extracts against ECHO viruses 1–14 (except 10) in monkey kidney cells. In general extracts were added to cells 24 hours before about 100 TCD50 of virus. An aqueous extract (called M2) of the fruiting body of *Calvatia gigantea* gave therapeutic indices of 1:28,800, 1:1,200 and 1:28,800 against ECHO 4, 9 and 11 respectively. The effect was measured by the presence or absence of cytopathic effects, not by titrating virus. The extract had no direct effect on virus. Increasing the dose of virus or delaying treatment of the cells greatly diminished the effect of M2 on ECHO 4 and 11. Cells protected against ECHO 4 and 11 remained sensitive to viruses not affected by M2. When 0·01 ml./gm. of M2 was given intraperitoneally to mice, and ECHO 4 or 11 viruses were also inoculated into them, it was found that the antibody titre was less in the treated mice than in controls given virus alone.

A. J. Beale

LOCKART, R. Z., Jr. **The Production and Maintenance of a Virus Carrier State: the Possible Role of Homologous Interference.** *Virology.* New York. 1960, Feb., v. 10, No. 2, 198–210. [14 refs.]

Strain L cells of a single clone were used. Inactive suspensions of western equine encephalitis virus were prepared by heating fluids containing 10^9 plaque forming units/ml. (PFU/ml.) at 37°C. for 100 hours. A minimum of 12 hours was required for this material to establish interference in L cells. 700–1,000 inactivated virus particles per cell were used and challenge was with 10–50 PFU active virus per cell. 10 or more PFU per cell caused complete degeneration of normal L cells in 3–6 days and surviving cells could only occasionally be recovered. 40 PFU of active virus simultaneously with an adequate dose of inactive virus caused only slight degeneration and complete recovery. Similar results were obtained by inoculating a suspension of 10^9 PFU which had been incubated until only 10^5 PFU remained active. 10^5 PFU active virus alone caused complete degeneration.

Immune serum, but not normal serum, was found to inhibit the interfering effect of inactive virus suggesting that an inactive virus/cell reaction occurs. However, cells protected by interference appeared to adsorb virus as well as normal cells. On challenge, cell layers protected by interference showed a variable degree of degeneration, their yield of virus was sharply diminished, and an increased proportion of the cells survived and were capable of clone-formation. When cells protected by inactive virus were trypsinized and made into monolayers, interference was found to persist through 2–5 generations of cell growth without addition of further inactive virus. Of protected cultures surviving challenge, 6 of 15 with nil to moderate degeneration became carrier cultures. Those with severe degeneration did not. The fluid from carrier cultures known to contain active virus caused little or no degeneration of normal L cell cultures and 5 of 7 of them became carriers. Carrier cultures contain 0·1–1·1 PFU of active virus per cell and it was estimated that 0·3–2·0% of the cells were infected. This virus was, however, of full virulence. The carrier state seems to be an equilibrium between interference due to inactive virus in the majority of the cells and active virus multiplication in a small minority.

C. E. Gordon Smith

KUO, Huei-Yü. **Tissue Culture Studies of Japanese B Encephalitis Virus. I. The Cytopathogenicity and Multiplication of the Virus in Monolayer Cell Culture of Chick Embryo.** *Chinese Med. J.* Peking. 1960, Jan., v. 80, No. 1, 21–7, 5 figs. (4 on 2 pls.) [22 refs.]

2 strains of Japanese encephalitis virus isolated from a man and a pig were studied in tube cultures of trypsinized chick embryo cells. After doses of 1,000–10,000 TCD50 of virus cytopathic changes started 2 days after inoculation. 10 serial passages were made and the titre varied from 4·7–5·2 log. The titre of virus in the cultures was maximal (10^6 mouse LD50) 2–4 days after inoculation and the titre fell thereafter.

C. E. Gordon Smith

MIMS, C. A. **Intracerebral Injections and the Growth of Viruses in the Mouse Brain.** *Brit. J. Exper. Path.* 1960, Feb., v. 41, No. 1, 52–9, 15 figs. (12 on 3 pls.) [14 refs.]

The Moscow strain of ectromelia and a low-passage strain of Murray Valley encephalitis were used in multicoloured (Melbourne) mice. Intracerebral inoculation of Indian ink revealed that most of the inoculum went directly into the bloodstream probably owing to destruction of the arachnoid villi. Ink was found throughout the subarachnoid space, in the Virchow-Robin spaces and in the ventricles, but not in the parenchyma except in the needle track and in fissures in the brain substance. Glial cells later appeared to carry ink to areas below the pia and ependyma. The pressures used in routine inoculations were found to be 200–300 cm. H_2O.

Extraneural inoculation of ectromelia gave titres in mouse brain of not more than 10^3 pock-forming units (pfu) per 0·05 ml. After intracerebral inoculation 10^6 pfu may result, but death appears to be caused rather by virus multiplication in the viscera. The same infectivity titres were obtained by parallel intracerebral and intravenous titrations. Fluorescent antibody studies and titrations of different parts of infected brains showed that ectromelia multiplies mainly in the meninges and ependyma and not in the parenchyma. Similar findings resulted with rabbitpox virus.

With mice inoculated intracerebrally with Murray Valley encephalitis, fluorescent antibody studies 4–5 days after infection showed that antigen was confined to the cytoplasm of parenchymal cells and was not present in meningeal or ependymal cells. Antigen was visible at 48 hours, but not 24 hours after infection. Murray Valley virus thus multiplies in the parenchymal cells which it may reach by being transported in wandering macrophages. *C. E. Gordon Smith*

POGODINA, V. V. **The Resistance of Tick-Borne Encephalitis Virus to the Effects of Gastric Juice.** *Problems of Virology.* London. 1958, v. 3, Nos. 5/6, 295–9, 1 fig. [Translated from Russian.]

The Fateev strain isolated from human blood following infection by tick bite, and the Ungemakht strain isolated from human blood after milk-borne infection were used. A 10% suspension of infected mouse brain in 3% serum saline was diluted 10-fold in the appropriate buffer: sodium-acetate-hydrochloric acid buffers from *p*H 1·42–4·95 and Sorensen buffers from *p*H 6·81–9·18. For inoculation into mice after various periods the *p*H was adjusted to *p*H 7·4–7·6. Marked falls in infectivity (around 4 log) were found within 5 minutes at *p*H 1·42 and within an hour at *p*Hs up to 3·95; the drop in titre was only slightly slower at *p*H 4·95. However, some infectivity persisted for up to 4 hours at *p*H 1·42 and up to 24 hours at *p*H 3·09. Some infectivity was found after 7 days at *p*H 4·95. At *p*Hs 6·81–9·18 there was little loss of titre up to 48 hours, but after 7 days the highest titre was at *p*H 7·73 and the lowest at 9·18.

Virus suspensions were next tested for survival in 24 gastric fluids with *p*Hs from 1·49 to 7·00. In all juices of *p*H 4·35–7·00 virus was present for at least 2 hours and also in most with *p*Hs 2·45–3·46. With lower *p*Hs most, but not all, juices were non-infective after 2 hours and some of them within 30 minutes. It thus seems probable that virus taken in milk and milk products is likely to pass through the stomach without complete inactivation in many individuals. [In the experiment with gastric juices the cause of death in mice inoculated does not seem to have been proven to be due to virus.] *C. E. Gordon Smith*

ANDONOV, P. S. **Pathogenicity of Tick-Borne Encephalitis Virus for Chicks.** *Problems of Virology.* London. 1958, v. 3, Nos. 5/6, 299–303, 2 figs. [Translated from Russian.]

The Ikh-10, IaS-8 and IM strains of virus were used. Chicks aged 3–5 days were inoculated intracerebrally with mouse brain suspensions. The incubation period in the chicks varied from 4–39 days. While some had rapidly fatal disease, others had a subacute remittent illness lasting up to 30 days. These birds were listless, trailed their wings, sometimes had paralysis, and were easily knocked over. Virus was isolated from birds in the acute stage (within the first 10 days), but not from those with subacute prolonged illnesses, except 1 bird from which virus was isolated 33 days after inoculation. Chicks are suggested as experimental models for study of subacute and chronic infections with tick-borne encephalitis viruses.

C. E. Gordon Smith

ILYENKO, V. I. & POKROVSKAYA, O. A. **Characteristics of the Course of Experimental Infection in Monkeys inoculated with Tick-Borne and Bi-Phasic Encephalitis and Louping Ill Viruses.** *Acta Virologica.* Prague. 1960, Mar., v. 4, No. 2, 75–81. [11 refs.]

FEDOROV, I. V. & TIUSHNIAKOVA, M. K. **Characteristics of a Strain of Tick-Borne Encephalitis Virus, isolated from the Tick** *Ixodes plumbeus* **Leach collected from Sand Martins.** *Problems of Virology.* London. 1958, v. 3, Nos. 5/6, 303–5. [Translated from Russian.]

83 sandmartins were caught in Tomsk in Western Siberia. On them were 4 larvae, 12 pupae and 36

imagos of *Ixodes plumbeus*. Virus isolations were attempted from the brains of the birds in 4 pools and from the ticks in 2 batches by intracerebral inoculation of mice. A virus was isolated from 1 pool of 37 ticks after 1 blind passage. The incubation period in mice was 10–14 days and the symptoms convulsions and paralysis. The virus was pathogenic for mice also by the intraperitoneal, intranasal and subcutaneous routes, but not for rabbits or guineapigs. It was found by a neutralization test to be identical with or closely re'ated to the Kargasokskii reference strain of tick-borne encephalitis virus. *C. E. Gordon Smith*

ŘEHÁCEK, J. **Experimental Hibernation of the Tick-Borne Encephalitis Virus in Engorged Larvae of the Tick** *Ixodes ricinus* **L.** *Acta Virologica.* Prague. 1960, Mar., v. 4, No. 2, 106–9. [16 refs.]

SALMINEN, A. **Difference in the Agglutinability of Rooster and Hen Erythrocytes by the Tick-Borne Encephalitis Virus.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1959, v. 37, No. 4, 400–406, 2 figs. [18 refs.]

A centrifuged alkaline saline extract of mouse brains infected with the Belyanchikov strain of tick-borne encephalitis virus was used as the antigen. Of erythrocytes from 26 roosters aged 1–4 years all gave haemagglutinin-titres of 12,800 to 25,600; of erythrocytes from 24 hens aged 1–4 years only 8 gave titres of 1,600 or over. These were compared with erythrocytes of 20 1-day-old chicks and 2 geese all of which gave titres of 12,800 to 51,200. When rooster, 1-day-old chick, and goose cells were compared over a range of temperatures from 4 to 37°C. and of *p*H from 6·0 to 7·0 there was no significant difference in titres. Optimum titres were obtained at *p*H 6·4–6·6 and at 4°C. The positively reacting hen cells had progressively narrower *p*H ranges of activity as the titres they gave diminished. Poor patterns were commoner with hen cells. Rooster cells were found to be satisfactory without addition of protein to the suspending solution. *C. E. Gordon Smith*

COLLIER, W. A., DE ROEVER-BONNET, H. & HOEKSTRA, J. Ueber Virulenz und Virulenz-Curven. [**Virulence and Virulence Curves**] *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1959, v. 25, No. 2, 113–36, 13 graphs. [15 refs.]

The authors propose a method for the graphic recording of the virulence of a virus. A number of experimental curves obtained with the 17D and Asibi strains of yellow fever virus are given in illustration of the method [see also *Trop. Dis. Bull.*, 1959, v. 56, 1122]. *D. J. Bauer*

MEERS, P. D. **The Desiccation of Yellow Fever Vaccine in a Modified Centrifugal Drying Plant.** *West African Med. J.* 1960, Feb., v. 9 (n.s.), No. 1, 29–32.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 584.]

HULL, R. N. & NASH, J. C. **Immunization against B Virus Infection. I. Preparation of an Experimental Vaccine.** *Amer. J. Hyg.* 1960, Jan., v. 71, No. 1, 15–28. [16 refs.]

A method was developed for the preparation of safe and potent vaccine against B virus infections. Failure of previous attempts in this direction are attributed to loss of virus antigenicity during the relatively long periods required for inactivation when low concentrations of formalin are used. For this reason attempts were made to prepare vaccines inactivated for 48 hours at 37°C. with formalin (37% formaldehyde) at a final dilution of 1/400. The virus material used for vaccine production consisted of fluids from infected rabbit kidney cultures. 10 batches of vaccine prepared by this procedure were exhaustively tested for the presence of residual infective virus, with consistently negative results. Potency tests based on antibody rises in rabbits, guineapigs and monkeys revealed good antigenicity which was best demonstrated in guineapigs. Vaccinated rabbits resisted large challenges with infective virus. Potency tests carried out in recently captured monkeys gave disappointing results mainly because of the frequent occurrence of natural infections among controls.

Methods for further increasing the safety of vaccines are suggested and the possible use for human vaccination is discussed. [See also PIERCE *et al.*, this *Bulletin*, 1959, v. 34, 507.] *H. G. Pereira*

ETCHEBARNE, M., BERNAL, P. G. & LEYTON, G. R. **Purification of Rabies Antibodies in Horse Serum and Diagnostic Importance of the Fluorescent Antibody Technique.** *J. Immunology.* 1960, Jan., v. 84, No. 1, 6–10, 2 figs. [32 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 590.]

IMMUNITY

GORECZKY, L. **Relations between Immune Substances and Protein Fractions.** *Acta Microbiologica.* Budapest. 1959, v. 6, No. 4, 307–14, 3 figs. [24 refs.]

Attempts to correlate antibody activity with particular protein fractions of serum indicated that not only gamma globulins but sometimes beta and even alpha globulins might act as antibody carriers. The author used a combination of paper electrophoresis and agar gel diffusion techniques to study the distribution of sheep cell haemolysins in rabbit serum and antistreptolysin in human serum and showed that the observed distribution of these antibodies among different serum

fractions varied with the amount of serum placed on the electrophoresis strip. With small quantities of serum (20–40 cmm.), antibody activity was confined to the gamma globulin fraction but extended to the beta and alpha globulins as the volume was increased (*e.g.* to 60–80 cmm.). The author suggests that use of excessive amounts of serum may be responsible for reported instances of antibodies associated with beta and alpha globulins. *John R. Norris*

HILLIGER, H. G. & HELLMANN, E. Analytische Untersuchungen von Kaninchenseren mit der Ultrazentrifuge nach Infektion oder Immunisierung mit Brucellen. [**An Analysis with the Ultracentrifuge of the Protein Composition of Rabbit Serum immune to Brucella**] *Ztschr. f. Hyg. u. Infektionskr.* 1959, v. 146, No. 2, 123–8, 1 fig.

The ultracentrifugal method of protein analysis has been used to compare the serum proteins of normal rabbits with those of rabbits immunized with *Brucella* antigens and shown to be rich in antibody.

The authors have been unable to demonstrate any significant qualitative differences between the normal and immune sera by this method although slight quantitative differences have been observed.

J. W. McLeod

HUANG, Nancy N. **The Antibody Response of Infants and Children to Vi Antigen.** *Amer. J. Hyg.* 1959, Nov., v. 70, No. 3, 275–9, 1 fig.

This study was undertaken in order to find out how LANDY's observations [this *Bulletin*, 1955, v. 30, 62] with regard to the antibody response of adults to a single injection of Vi antigen compared with the response of infants and children to similar procedures. It was found that among 27 infants of 6 months or less only 4 responded with antibody formation to a single subcutaneous injection of 0·04 mgm. purified Vi antigen prepared from *Escherichia coli*. Infants of one year or over responded in much the same way as older children and adults. Landy found that repeated injections of the Vi antigen preparation failed to push up the Vi antibody response in adults and the present author found that this was equally true for children and young infants. The persistence of Vi agglutinins for relatively long periods (20 months or more) reported by Landy is confirmed. *H. J. Bensted*

WAHLIG, H. Properdin-System und Antikörperbildung. I. Der Serum-Properdinspiegel von Kaninchen während der Immunisierung mit *Mycobacterium tuberculosis*. [**The Properdin System and Antibody Production. I. Serum Properdin Levels in Rabbits during Immunization with** *M. tuberculosis*] Reprinted from *Arch f. Mikrobiol.* 1959, v. 32, 127–37, 3 figs. [25 refs.] II. Der Serum-Properdinspiegel von Kaninchen während der Immunisierung mit *Salmonella typhosa*. [**II. Serum Properdin Levels in Rabbits during Immunization with** *Salmonella typhosa*] *Ibid.*, 322–7, 3 figs. [11 refs.]

I. A modification of McNall's method of estimating properdin was used, in which zymosan was substituted for inulin, and antibody to the *Myco. tuberculosis* was determined by the MIDDLEBROOK-DUBOS [this *Bulletin*, 1949, v. 24, 278] method of agglutination of antigen-sensitized red blood corpuscles. The estimation of the albumin and various globulins in the sera was determined by paper electrophoresis according to the recommendations of GRASSMANN and HANNIG.

Properdin was found to rise sharply to a maximum on the 4th day and to fall away to a minimum about the middle of the third week. The antibody titre rose sharply about the middle of the second week and remained at a high level during the period of observation, 7 weeks. The gamma globulin rose more slowly but had reached a high level about the time of the properdin minimum. It continued to rise slowly during the period of the experiment.

The *Myco. tuberculosis* resembled zymosan in capacity to bind properdin and inactivate complement.

II. In these observations the methods followed were as in the first except that titration of antibody to *Salmonella typhosa* was by slide agglutination with progressive dilutions of serum.

The properdin in this series, after a slight and brief preliminary rise, sank to a minimum about the third day and then rose to a maximum, 120% of the original level, about the eleventh day, after which it gradually fell to the normal level. The attainment of maximum properdin level coincided with the period of most rapid rise of antibody titre, but from the end of the second week the properdin fell while antibody increased.

The rise of antibody titre began about the second day and, rising sharply for the first fortnight, continued to rise more slowly until the end of the experiment in the fourth week. *J. W. McLeod*

TURK, J. L. **Further Observations on the Nature of Some Antibody-Like Activities in Normal Human Sera.** *Brit. J. Exper. Path.* 1959, Dec., v. 40, No. 6, 578–82. [13 refs.]

The author has previously described [this *Bulletin*, 1959, v. 34, 1308] the finding in human and other sera of specific and non-specific antibody-like substances which can be shown to react with starch and various bacteria by the immune adherence reaction [*ibid.*, 509]. The chemical nature of these substances has now been investigated by fractionating 8 human sera by treatment with ethanol in the cold, and testing each fraction for immune-adherence activity against starch, *Salmonella typhi*, *Shigella flexneri*, *Escherichia coli*, *Vibrio El Tor*, and *Staphylococcus aureus*.

The active fraction was that left after the removal of albumin and most of the alpha and beta globulins. It appeared to be a beta globulin. Ultracentrifugation of a fraction containing alpha 2, beta and gamma globulins showed that a major component of the active agent remained in the supernatant with the lighter globulins after the heavy globulins, including properdin and anti-A haemagglutinins, had sedimented as a pellet. Addition of the supernatant to the pellet,

the combined individual activities of which were less than that of the uncentrifuged material, restored activity to the original level. This suggested that a co-factor acting along with properdin was necessary for full activity. Treatment of serum with cysteine abolished its activity against all the antigens except *Staph. aureus* and *V. El Tor.* This was considered to indicate the destruction of properdin but not of specific antibody. *I. B. R. Duncan*

VAN TRIET, A. J. **Enzymatic Purification of Anti-diphtheria and Antitetanus Sera obtained from Sheep.** *Brit. J. Exper. Path.* 1959, Dec., v. 40, No. 6, 559–66. [14 refs.]

Antisera for diphtheria and tetanus toxins which had been obtained from sheep have been investigated from the standpoint of enzymatic purification. A detailed scheme of the steps in such a preparation is given and contrasted in respect of the strength of reagents, temperatures of exposure, etc. with those which give the best results with horse antisera.

The purified product obtained by the method adopted was adequate in respect of titre and of the ratio of potency to protein content, although not so good as the purified horse sera in these respects. It had also lost a very large part of the species-specific protein present in the crude toxin from which it was obtained.

Results obtained with antitetanic sheep sera were rather better than those with the antidiphtheritic sera.

There was a marked diversity, however, between the titre as determined by the Ramon flocculation method *in vitro* and a skin sensitivity test *in vivo.*

The advantages of having a second serum available is obvious in avoiding anaphylactic reactions and the unduly rapid elimination of foreign protein if a second injection of the same serum is given after an interval of time. *J. W. McLeod*

Miscellaneous

AUDY, J. R. **Delivery of Papers at Congresses and other Meetings.** *Med. J. Malaya.* 1959, Sept., v. 14, No. 1, 1–11, 2 figs.

Audy takes this subject seriously—*O si sic omnes*—because "A high proportion of papers read at formal scientific meetings fail to carry their full messages and some fail almost completely". A speaker may wish to appeal to the specialist in his field, to a specialist in another but related field, or to a worker in another field, and special attention should be paid to the last two. The paper should educate, entertain and challenge.

Defects include poor vocal delivery, reading material prepared for printing and not for speech, too much detail or jargon, poor handling of slides, and poor preparation of slides. It is essential to prepare 2 papers—one for publication and the other (simpler) paper for the actual speech. The latter can easily be spoiled by too much detail, or by over-elaboration, or by presentation in confusing order, or by overestimating the capacity of the audience to assimilate facts. It is unforgiveable to exceed the allotted time.

Visual aids are meant to support, amplify or replace the spoken word, and should be used at appropriate moments. Slides containing words or figures should always be easily legible and should not be overcrowded.

This useful paper should be required reading for everybody who speaks at a scientific meeting. *Charles Wilcocks*

Book Reviews

WORLD HEALTH ORGANIZATION. PUB. HEALTH PAPERS No. 2. **Epidemiological Methods in the Study of Mental Disorders** [REID, D. D. (M.D., D.Sc., M.R.C.P.)]. 79 pp. 1960. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [5s.; $1.00; Sw.fr. 3.–.]

In this short but densely packed monograph Professor Reid has not only set forth the basic principles of epidemiological enquiry; he has also, by means of judicious illustrations, shown "the practical problems most often encountered in the design, conduct, and interpretation of epidemiological studies of mental disorder". By so doing, he explains in his foreword, he hopes "to spare the novice in the field some of the disappointments and frustrations which might prevent his going on to do useful work".

Some 70 pages later, in a postscript to his book, the author reflects that his review of past work in this field may seem to have been hypercritical; but he remains unashamedly a stickler for the utmost attainable rigour in the conduct of epidemiological studies.

If rigour is harder to attain in psychiatric than in other forms of medical enquiry then, he implies, so much the worse for psychiatrists. If the revelation of the difficulty of the task deters the novice from even starting, we may be spared from having to read another inconclusive and basically uninformative contribution to a literature in which such false starts have been all too numerous.

On the other hand, if the beginner is made of sterner stuff, he will find in this monograph not only awful warnings of the pitfalls in his path but also sound advice (backed up by a selective bibliography) on how to circumvent them. The first challenge which epidemiological enquiry presents to the psychiatrist is to find reliable indicators of mental illness. In most other types of disease one would demand *objective* as well as reliable indicators; but in the majority of psychiatric disorders, diagnosis has tended to lean heavily upon the psychiatrist's assessment of each case, with all its attendant risks of subjective bias. This need not always be the case. From his own war-time experience, Professor Reid is able to illustrate the way in which simple measurable data, such as the number of errors in navigational plots, or the aircrew member's weekly weight record, could serve as indicators of impending emotional breakdown.

The classical criterion for recognition of a case has been the fact of admission to a mental hospital. In spite of the well-known limitations of such data (which were clearly described by Esquirol more than a century ago) they can be of use in countries where both record-keeping and provision of hospital facilities have been consistently maintained at a high level. In interpreting differences in rates of admission to hospital from different sections of a population one cannot, however, confidently make inferences about aetiological factors: it often appears that the differences reflect features of prevailing psychiatric practice, or local variations in attitudes towards consulting psychiatric help rather than true differences in rates of appearance of the illness.

As always in epidemiology, studies of hospital populations only whet the appetite for field surveys which will measure the true incidence of disease in the general population. Here Professor Reid traces the increasing sophistication of studies from those done by the school of Rudin, and by Brugger in Germany in the late nineteen-twenties, through the examplary Scandinavian genetic surveys of Strömgren, Fremming and Böök, to the recent American studies which have combined sociological and psychiatric assessments of the populations under review. Here his illustrations show the psychiatrist's discovery, first of the importance of the demographic characteristics of the population studied, then of how to safeguard against sampling errors and finally—because this is a problem which is still far from solution—of the difficulty of achieving reliable measures of mental morbidity and of social attributes. As the narrative unfolds, more and more sources of error are revealed: the interplay of genetics, of environment, of physical illness, of selective migration becomes so complex that one begins to doubt the interpretations advanced in the reports of even the best-conducted field studies.

Through the general gloom a few gleams of hope are offered by the success of a number of prospective studies which have followed particular groups of subjects and controls over a limited period of time. The virtue of these studies is that they have focussed deliberately upon a few elements at a time; but even here the warning note is heard: "Observer bias is of particular importance in the intimate context of psychiatric history-taking, and the personal bias of the interviewer is almost bound to be reflected in the persistence with which he pursues his favourite topics among the sick propositi."

One detects here, and very occasionally elsewhere in the text, a note of petulance with the obdurate subjectiveness of psychiatric interviewing—a reminder that the author is an epidemiologist and not a psychiatrist. He has shown remarkable forbearance in excluding from his references any instances (which would not be hard to find) of psychiatrists' unfamiliarity with the elements of scientific method, or of their conspicuous failure to reach agreement even in the classification of the conditions which they treat.

What Professor Reid has done, however, is to state explicitly, and with instances, the requirements of epidemiological enquiry, if this is to be used as a scientific discipline: in so doing he presents a challenge to the psychiatrists to devise means of systematizing their clinical observations so that they too can profit from this field of research. *G. M. Carstairs*

DEWBERRY, Elliot B. [M.B.E.] **Food Poisoning: Food-Borne Infection and Intoxication. Nature, History, and Causation. Measures for Prevention and Control.** 4th Edition. Foreword by Sir A. MACNALTY, K.C.B., M.A., M.D., F.R.C.P., F.R.C.S., D.P.H., F.R.S.E. pp. xvi + 411, 40 pls, 16 text figs. 1959. London: Leonard Hill [Books] Ltd., Leonard Hill House, Eden Street, N.W.1 [45s.]

This book has been well known and consulted by public health workers for many years [this *Bulletin*, 1950, v. 25, 1324]. We are grateful, therefore, for the 4th edition which includes the contents of the previous book as well as much up-to-date material. It is useful to find in one volume references giving the historical facts on food poisoning from early in the 19th century up to 1957; in addition the new book includes statistical data taken from the annual reports on food poisoning published in the *Monthly Bulletin of the Ministry of Health and Public Health Laboratory Service*. It is good to note that Dewberry emphasizes the importance of animal sources of salmonellae although the present trend towards the consideration of the animal carrier as of equal if not greater importance than the human carrier is not new, as may be seen from earlier work described by Dewberry.

The growth of knowledge on the carriage and excretion of salmonellae by animals and birds, particularly calves and poultry, and data on the salmonella content of foodstuffs of animal origin such as eggs

meat, and protein meals for animal feeding-stuffs, give the veterinary epidemiologist a vital part to play in tracing the spread of contamination to and around the farm, and from the farm through dealers, markets and abattoirs. The public health epidemiologist continues the search through manufacturing establishments, shops, canteens and homes. [The bacteriophage typing of certain salmonella serotypes, particularly *Salmonella typhi-murium*, has increased the value of epidemiological studies.]

Environmental hygiene described in Chapter X by Cecil Ash (pp. 165–186) is important not only for preventing the spread of infection from human and animal carriers to foodstuffs, but also for suppressing the spread of intestinal pathogens from foodstuffs allowed to contaminate working surfaces, utensils and cloths, to other foods which may not require to be cooked.

It is good also to see a small chapter devoted to *Cl. welchii* food poisoning (pp. 129–133), the incidence of which continues to be 80–90 recorded outbreaks yearly; the value of correct cooking, cooling and storage techniques, as preventive measures, is strongly emphasized.

The information about staphylococcal enterotoxin food poisoning (pp. 134–164) re-emphasizes the human carrier as the main source of coagulase-positive staphylococci, and examples of outbreaks are given. The difficulty of detecting enterotoxin in the absence of the organism is stressed. [It may be mentioned that Professor Dack and his colleagues in Chicago are now working on a precipitin test for the detection of enterotoxin-producing staphylococci in the presence of antitoxin prepared from purified enterotoxin; they have found 2 distinct antigenic types of enterotoxin.]

Although food poisoning from metallic salts (pp. 187–229) has not figured largely in the annual returns for food poisoning in recent years, it is nevertheless interesting to learn the potential dangers. Much valuable information is also given in the chapters on poisonous plants, fungi, fish and shellfish. These chapters, together with the account of food allergies, provide a useful compilation of data on causes of food poisoning other than those due to microbiological agents.

The subject of botulism is treated thoroughly; Part IV (pp. 294–344) includes a historical review, description of symptomology and causation, data on the heat-resistance of the spores of *Clostridium botulinum* and toxin-antitoxin reactions, a description of the types of food associated with outbreaks of botulism with illustrative outbreaks, and a concluding chapter on prevention and control.

In the chapter *Canned Foods and their Inspection* (pp. 345–362), Cecil Ash gives a clear and simple picture of processing techniques and the methods used to detect major faults.

Part VI deals with the laboratory investigation of food poisoning, including methods of isolation and identification of salmonellae, staphylococci, *Cl. welchii* and *Cl. botulinum* from foods, stools and vomit; the formulae for many media are given.

[Recent work has proved the value of the Wilson and Blair bismuth sulphite agar and the use of 25 gm. quantities of food in liquid enrichment media when searching for salmonellae.]

Appendix I (pp. 383–399) gives in full *Steps to be taken in England and Wales by Medical Officers of Health in the Investigation and Control of Food Poisoning*, as published in 1949 by H.M. Stationery Office. Appendix II (pp. 400–402) summarizes methods to control gastro-enteritis on ships. [Recent experiences indicate, however, that intestinal pathogens may be introduced into the galley from foodstuffs as well as from carriers, and that attention should be given to spread of contamination from one food to another *via* equipment and utensils; furthermore it is not easy to obtain a correct record of foods eaten from well-filled menus.]

Altogether this is a most useful and comprehensive text-book, simply and clearly written, and should be in the possession of all those interested in the bacteriology and epidemiology of food-borne infection. *Betty C. Hobbs*

Elek, Stephen D. [M.D., D.Sc., Ph.D., D.P.H.] *Staphylococcus pyogenes* **and its relation to Disease.** pp. vii + 767, numerous illustrations, 1959. Edinburgh, London: E. & S. Livingstone, Ltd. [84s.]

The general concern regarding staphylococcal infections is readily evident from the amount of attention which it received in medical and scientific journals published throughout the world. The volume of work carried out on *Staphylococcus aureus* over many years has been great and the disciplines employed diverse. In order that ideas might be shared among specialists in different fields of knowledge an attempt has been made in this book to provide a comprehensive bibliography of the most important papers concerned with this pathogen.

To the reviewer it seems that this book will be invaluable to all research workers who work with staphylococci and to medical bacteriologists as a work of reference. One might quibble with the author when he says that he tried to collect "the most important papers", because it would appear that on the topics he chose to deal with he made a list of all the relevant papers, as a rough tally reveals that there are quoted about 4,000 references. The text of the book runs to 529 pages and consists of a fluent and coherent account of the organism—is morphology, physiology, antigenic structure, reaction to bacteriophage, pathogenicity and susceptibility to antibiotics.

It is obviously extremely difficult for any one person to assess the significance of fundamental work in spheres as diverse as biochemistry, genetics, physiology, and epidemiology, and it appears that in some chapters the style is largely descriptive. On the other hand where the author is dealing with the virulence of the organism, and with its products thought to be capable of playing a role in the pathogenic process, a subject which is the province of a medical bacteriologist, not only does he state the facts clearly and in a well-ordered manner, but he also gives his own views. It is difficult to find fault with the chapter on staphylocoagulase or that on diffusible products. On the other hand he gives

the impression that the study of pathogenicity of staphylococci by reference to experimental infections in laboratory animals is unlikely to be fruitful.

The author is at pains to point out that virulence of staphylococci for animals does not indicate virulence for man and goes on to say, "It is conceivable that the elements responsible for virulence differ among various animals, and conclusions drawn from mice are notoriously difficult to apply to man". These points must be accepted, but even so it is possible that animal experiments may provide useful models for the study of pathogenicity which may throw some light on human disease. An example of Professor Elek's criticism of animal experiments is that death of rabbits following intravenous injection of staphylococci merely indicates the *in vivo* production of the lethal toxin. He does not give justification for this statement and indeed he later states that the (lethal) alpha toxin may not play a decisive part in virulence to rabbits. An approach more favoured by the author is the experimental infections in humans. This, apart from obvious disadvantages, may also be highly artificial since the number of organisms necessary to cause a small pustular lesion in the skin is 7×10^6, an inconceivably large dose for a natural infection. The conclusion that neither human nor animal experimental infections are fully satisfactory seems, therefore, inevitable. It appears to the reviewer that the potential value of animal experiments in assessing the important factors known and unknown has been too readily dismissed.

Again, it is difficult to agree with his statement "the failure to obtain cures with antitoxin strongly suggests that the known toxins are not the essential factors in virulence". Although he is certainly correct in saying that alpha toxin does not play the same part as does diphtheria toxin in diphtheria, it may yet make some vital contribution to the pathogenic action of the micro-organism.

Staphylococcal virulence, and resistance to infection, are reviewed in detail and although it is possible to take issue with the author on some of his views this unwieldy subject has been presented in an orderly and informative manner. The position regarding present knowledge is summed up by the statement ". . . the nature and role of the agents enabling staphylococci to survive and multiply in human tissues are ill understood. In all probability no single factor is of overriding importance".

The scope of the book did not allow reference to the many papers dealing with clinical aspects of disease, but in the last chapter entitled *Clinical Problems of Staphylococcal Infection* there is a most useful discussion regarding the causation and possible means of controlling hospital sepsis.

The reasons for recommending this book are threefold. Firstly it is easily read, secondly the extensive bibliography will be of the greatest value to all workers in this field, and finally problems are defined in a manner likely to provoke further contributions to the study of staphylococci. *Douglas D. Smith*

Notice

Consideration has from time to time been given to the question whether it would be desirable to include authors' addresses in the headings of abstracts in the *Bulletins* and it has been decided that the additional time and cost involved would not be justified. Subscribers are advised, however, that the Bureau will, on request, notify them of the name and address of the author of the article, or the publisher of the journal, from which an abstract has been made.

The Bureau also deals with enquiries from individual subscribers relating to abstracts which have appeared in the *Bulletin of Hygiene* and the *Tropical Diseases Bulletin*; correct references and the exact nature of the information required should be stated.

Printed in Great Britain by The Eastern Press, Ltd., London and Reading